

THE BRITISH JOURNAL OF DERMATOLOGY JANUARY 1953

THE RELATION OF DEFICIENCIES OF VITAMIN A AND OF ESSENTIAL FATTY ACIDS TO FOLLICULAR HYPERKERATOSIS IN THE RAT.*

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HYPERKERATOSIS of the hair follicles resulting in a papular eruption of the skin has been known to dermatologists for nearly a century to be present in a variety of skin diseases such as pityriasis rubra pilaris of Devergie (1857), keratosis follicularis of Darier (1889) and White (1889), lichen pilaris seu spinulosus of Crocker (1888), keratosis follicularis contagiosa of Brooke (1892) and keratosis pilaris of Brocq (1893). The first clear-cut description of an association between papulofollicular lesions of the skin and nutritional deficiency was given by Stannus in 1912. It is nearly two decades since Frazier and Hu (1931) in China, Loewenthal (1933) in East Africa and Nicholls (1933) in Ceylon independently suggested an aetiological association between deficiency of vitamin A and a similar papular eruption of the skin to which Nicholls (1933) gave the name phrynoderma. In further studies these authors obtained more evidence considered to support the hypothesis of deficiency of vitamin A (Frazier and Hu, 1934, 1936; Frazier and Li, 1938; Frazier, Hu and Chu, 1943; Loewenthal, 1935; Nicholls, 1934, 1935; Nicholls and Nimalasuriya, 1939, 1940). The observations of Goodwin (1934), Radhakrishna Rao (1937, 1938), Jeghers (1937), Youmans and Corlette (1938), Sequeira (1938), Pemberton (1940), Lehman and Rapaport (1940) and Fasal (1944) were believed, in the main, to support this hypothesis. Many dermatologists accepted the validity

* The results of this work were demonstrated to the British Association of Dermatology on 30 June, 1951, and were reported to the Nutrition Society on 26 May 1951 (Ramalingaswami and Sinclair, 1951).

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of these findings (Sutton and Sutton, 1939; Sequeira *et al.*, 1947; Ormsby and Montgomery, 1948; Andrews, 1938, etc.), and most nutritionists accepted the skin lesion as a sign of malnutrition in public health work. The supposition of deficiency of vitamin A appeared to receive support recently from the gratifying results obtained in the treatment of some cases of Darier's and Devergie's diseases with massive doses of vitamin A (Peck *et al.*, 1941, 1943; Barwasser, 1941; Cannon, 1941; Sweitzer, 1942; Michelson, 1942; Abramowitz, 1942; Carleton and Steven, 1943; Welton, 1943; Newman, 1943; Leitner and Moore, 1946; Porter and Godding, 1945; Porter *et al.*, 1947; Pettler, 1936, 1942; Brunsting and Sheard, 1941; Peck and Chargin, 1941; Weiner and Levin, 1943; Cornbleet *et al.*, 1944). At the present time there is much interest in the supposed relationship between deficiency of vitamin A and hyperkeratinization of follicular epithelium.

In recent years, however, there has been a gradual accumulation of some critical observations which throw serious doubt on the validity of this hypothesis. Aykroyd and Rajagopal (1936), during a nutritional survey of about 2000 South Indian schoolchildren, observed no correlation between the incidence of Bitot's spots and phrynoderma. Although Steffens, Bair and Sheard (1939, 1940) reported the production of follicular hyperkeratosis in human volunteers deprived of vitamin A, a similar study in 1942 by the Oxford Nutrition Survey and the more recent study of the Medical Research Council (1949) failed to reveal any follicular lesions. It is significant that in long-standing cases of coeliac disease proved by blood analyses and absorption curves to be markedly deficient in vitamin A, Sinclair (1945) did not find any follicular hyperkeratosis. Gopalan (1947) observed no improvement in five cases of phrynoderma treated with a concentrate of vitamin A for about six weeks. Stannus (1945) has maintained that the follicular hyperkeratosis observed in the malnourished populations of the East is none other than keratosis pilaris so commonly seen in the West, and that it has no primary aetiological relationship to deficiency of vitamin A. It is also of interest that epidermal and follicular tissues do not appear to contain vitamin A (Cornbleet and Popper, 1942).

Other nutritional upsets have from time to time been suggested as aetiological factors. Several cases of follicular hyperkeratosis in association with signs of deficiency of the B complex were recorded (Stannus, 1912; Platt and Gin, 1935; Reiss, 1936; Gopalan, 1947), and marked improvement in nine cases treated with yeast extract was reported (Gopalan, 1947). Many of Nicholls's original cases of phrynoderma also had sore mouth (Nicholls, 1934). In a review in 1942 Wolbach and Bessey went so far as to imply that all cases of phrynoderma were due to deficiency of riboflavin. However, riboflavin as well as nicotinamide were found to be inactive in the treatment of phrynoderma (Gopalan, 1947), and Aykroyd and Krishnan (1937) found no correlation between the incidence of phrynoderma and angular stomatitis.

There is no doubt that in spontaneous and experimentally induced scurvy in man a similar papulofollicular lesion occurs early in the deficiency (Nicolau, 1918; Wiltshire, 1919; Aschoff and Koch, 1919; Scheer and Keil, 1934; Crandon *et al.*, 1940); but sooner or later perifollicular haemorrhages—so characteristic of the scorbutic lesion—appear, and this important sign is agreed by all workers not to occur in phrynoderma.

From the information obtained by diet surveys, a deficiency of fat in the diet has been suggested as an important aetiological factor (Aykroyd and Rajagopal, 1936). Hawes (1945) believed that a relative dietary deficiency of fat to carbohydrate was probably responsible. More recently, Gopalan (1947) claimed good results in four out of six cases of phrynoderma from treatment with linseed oil, and in the last few months, while the present investigation was in progress, Menon *et al.* (1950) reported a lowering in the degree of unsaturation of plasma lipids in cases of phrynoderma which subsequently showed clinical and biochemical improvement on oral treatment with sesame oil.

PURPOSE OF THE PRESENT STUDY.

From this brief review of the clinical literature on phrynoderma the present lack of agreement on its precise aetiology is obvious. An experimental approach in which precise observations can be made and specific uncomplicated deficiencies can be produced is urgently required to decide whether or not a lesion resembling phrynoderma could be produced in experimental animals by dietary means. Although much valuable information on the skin changes in several acute vitamin deficiencies is available, largely through the work of Sullivan and his colleagues, certain gaps in our knowledge have remained which prevent us from integrating the experimental background to its aetiology. The object of the present study was to obtain experimental evidence that would throw light on its aetiology, taking especially into consideration the various factors that are known to be of importance in the genesis of the lesion in man. The rat has been used in all experiments, and the changes in the skin of the anterior abdominal wall were studied throughout for comparison.

A study of the clinical literature shows that, apart from plain deficiency of calories, deficiencies of vitamin A, of fat and of B vitamins, either singly or in combination, might be important in the aetiology of phrynoderma. Deficiency of vitamin A is the oldest and most widely accepted hypothesis, to which further support was given by Moul't's claim (1943) that the skin changes in rats deficient in vitamin A were identical with those in phrynoderma. Sullivan and Evans (1943, 1945), however, were not convinced of the identity of the two although they also observed a general similarity between them. In their classical monograph on deficiency of vitamin A in the rat, wherein the concept of keratinizing metaplasia of lining epithelium was first enunciated, Wolbach and Howe (1925)

mentioned finding only slight atrophy of the hair follicles and sebaceous glands in the skin of the eyelids—the only part of the skin examined. All these workers conducted relatively short-term experiments using recently weaned rats. It is doubtful if such experiments have their exact counterpart in the naturally occurring condition of phrynoderma. Endemic nutritional disease in man is very often the result of chronic insufficiency rather than complete lack of one or more nutrients and the structural consequences in the two cases might be different. Another important clinical feature to which insufficient attention has been paid is the marked predominance of phrynoderma in adolescence at a time when the pilosebaceous follicle is undergoing active development and hormonal influences are playing a part. Selye (1943) made the interesting observation that oestradiol applied locally to a strain of hairless mice resulted in marked hyperkeratosis of the rudimentary hair follicles and atrophy of sebaceous glands. Taking these factors into consideration we have investigated in four experiments the relationship between deficiency of vitamin A and follicular hyperkeratosis.

The second factor, fat deficiency, is important because whenever phrynoderma has been treated with vitamin A and cures claimed, fatty acids have also been administered, thus making it imperative to study the structure of the pilosebaceous follicles in deficiency of fat. No information on this point was available in the literature, although the syndrome of deficiency of essential fatty acids in the rat was clearly recognized by Burr and Burr in 1929. Williamson (1941), who examined the skin of three fat-deficient rats microscopically, described surface hyperkeratosis, but made no mention of the hair follicles, sebaceous glands and corium. In the fifth experiment we have investigated the effect of deficiency of essential fatty acids on cutaneous structure.

Of the B vitamins, studies of the skin changes in deficiencies of riboflavin, pantothenic acid and biotin (Sullivan and Nicholls, 1941, 1942*a* and *b*) revealed no resemblance to the lesion in phrynoderma, except that in the early stages of deficiency of biotin there was some follicular hyperkeratosis; they have not therefore been investigated by us. In view of the functional inter-relationships of pyridoxine and the essential fatty acids (Birch and György, 1936; Birch, 1938; Richardson and Hogan, 1936, 1941; Salmon, 1938, 1941; Quackenbush *et al.*, 1942), the skin changes in deficiency of pyridoxine were studied by us in the sixth experiment.

DEFICIENCY OF VITAMIN A.

Experimental Procedure.

Animals.—In Experiment I, which may be called acute deficiency, deficiency of vitamin A was induced in weanling rats. The vitamin was withdrawn completely from the diet of the deficient animals throughout the experimental period of ten weeks. In Experiment II (chronic deficiency), in which weanling

rats were again used, the deficient animals were given a dose of 250 i.u. of vitamin A at the end of each period of depletion and were thus maintained for over 24 weeks. The control animals in both these experiments received 1000 i.u. of vitamin A every week and were pair-fed with their corresponding deficient animals.

In Experiment III partial deficiency was induced in eight-weeks-old adolescent rats. Four groups were maintained respectively on 0, $\frac{1}{3}$, $\frac{2}{3}$ and 3 times their supposed minimum requirement of vitamin A for about twelve weeks. In Experiment IV partial deficiency was induced in weanling rats by the same procedure as in Experiment III. Details of the design of these experiments are given in Table I.

TABLE I.—*Experimental Details of Vitamin A Deficiency.*

Experiment number.	Type of study.	Weekly amount of vitamin A.	Animals used.			Duration of experiment (weeks).
			Number.	Age at beginning of experiment (weeks).	Strain.	
I	Acute	1. Nil	6	3	Albino	10
		2. 1000 i.u.	6			
II	Chronic	1. Nil*	7	3	"	24
		2. 1000 i.u.	7			
III	Partial	1. Nil	8	8	"	12
		2. 2 i.u.	8			
		3. 4 i.u.	8			
		4. 20 i.u.	8			
IV	"	1. Nil	12	3	Hooded	14
		2. 1 i.u.	12			
		3. 2 i.u.	12			
		4. 10 i.u.	12			

* 250 i.u. vitamin A given intermittently after 8 weeks of deficiency.

Based on the work of Goss and Guilbert (1939), the minimum requirement of vitamin A was taken as 20 i.u. of vitamin A per kg. of body weight, and the amounts to be fed to each group in Experiments III and IV were calculated on the basis of their average initial weights. These amounts were kept constant throughout the experimental period, with the result that as the animals grew, the amount of vitamin A given became gradually less than the stated proportion of their requirements.

Diet and supplements.—All animals in both deficient and control groups were fed on a basal vitamin-free diet of the following percentage composition :

Rice starch	63.0
Casein (fat- and vitamin-free)	21.0
Vegetable oil	10.5
Salt mixture (Hegsted <i>et al.</i> , 1941)	5.5

The animals in Experiments I and II received the following amounts of water soluble vitamins daily by mouth independent of food :

Thiamine hydrochloride	0.1	mg.
Riboflavin	0.16	„
Nicotinic acid	1.0	„
Pyridoxine hydrochloride	0.1	„
Calcium pantothenate	0.2	„
Biotin	0.002	„
Inositol	2.0	„
Choline chloride	10.0	„
Para-aminobenzoic acid	1.0	„
Pteroylglutamic acid	0.02	„
Vitamin K ("Synkavit")	0.1	„

In Experiments III and IV the water-soluble vitamins were mixed in the basal diet in the following proportions :

	Per 100 g. of basal diet.
Thiamine hydrochloride	1.0 mg.
Riboflavin	1.6 „
Pyridoxine hydrochloride	1.0 „
Calcium pantothenate	2.0 „
Nicotinic acid	10.0 „
Choline chloride	100.0 „

All animals received 5.0 mg. of L-tocopherol and 50 i.u. of vitamin D each week separately by mouth.

Methods.—The animals were weighed every week, and a general clinical examination and an examination of the eyes with a slit-lamp microscope were made at frequent intervals. They were killed by sharply cutting through the neck in order to collect blood for investigations, and were opened immediately afterwards. The internal organs were examined macroscopically, and samples of relevant organs fixed in 10 per cent. formol-saline for histological studies. The skin from the trunk and limbs was removed by using a sharp scalpel and cutting perpendicular to the surface and was also fixed in formol-saline. The parts of skin were cleared in xylene and embedded in paraffin ; sections were cut 6 to 8 μ thick perpendicular to the surface and stained routinely with Ehrlich's haematoxylin and eosin, Weigert's haematoxylin and van Gieson, Masson's trichrome and Heidenhain's haematoxylin stains.

Results.

General pathology.—The clinical course and structural changes in the deficient animals were similar to the well-known effects of deficiency of vitamin A in the



FIG. 1.

FIG. 1.—Section through the posterior part of the tongue of a control rat showing normal appearance of acini and ducts of the accessory salivary glands. $\times 60$.

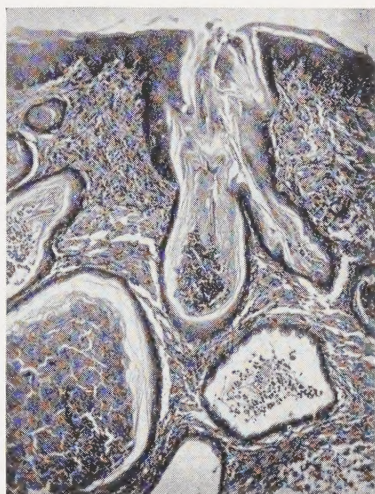


FIG. 2.

FIG. 2.—Section through the posterior part of the tongue of a vitamin A-deficient rat showing severe keratinizing metaplasia of lining epithelium of ducts. The ducts are distended with keratotic lamellae, and there is polymorphonuclear infiltration in and around them. $\times 60$.

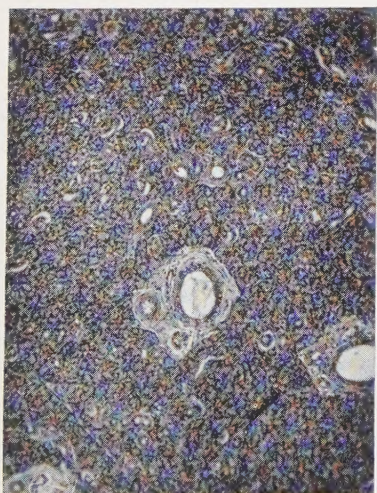


FIG. 3.

FIG. 3.—Sub-maxillary salivary gland of a control rat showing normal-looking ducts, acini and interstitial tissue. $\times 60$.

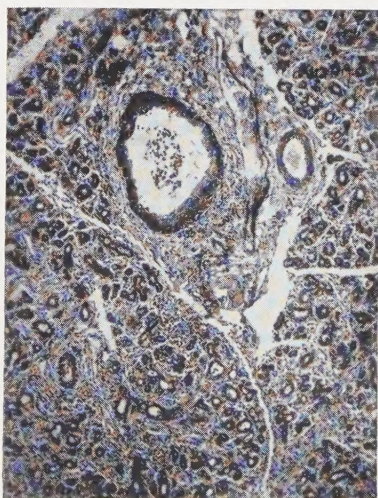


FIG. 4.

FIG. 4.—Sub-maxillary salivary gland of a vitamin A-deficient rat showing keratinizing metaplasia of lining epithelium of a large inter-lobar duct with leucocytic infiltration in and around it. There is also a mild diffuse leucocytic infiltration of the interstitial tissue of the gland. $\times 60$.

mammal, and will not therefore be repeated here. The features included: failure of growth; dental depigmentation; rough and "blotchy" appearance of fur; conjunctival hyperkeratosis; keratinization, oedema, vascularization and necrosis of the cornea; degeneration of the layer of rods and cones and vacuolation of the layer of pigment epithelium of the retina. In addition, many of the internal organs of the deficient animals showed structural changes in their lining epithelia, of which keratinizing metaplasia was the keynote (Figs. 1 to 4). The amount of vitamin A in the liver and plasma of some of the animals in Experiments I and II was determined by the Carr-Price reaction (Sinclair, 1947). The results presented in Table II show the extreme state of depletion

TABLE II.—*Plasma and Liver Vitamin A Values in Experiments I and II; Deficiency of Vitamin A.*

		Experiment I.		Experiment II.	
		Plasma.	Liver.	Plasma.	Liver.
		(I.u./100 ml.)	(I.u./g. wet weight.)	(I.u./100 ml.)	(I.u./g. wet weight.)
Pair 1:	Deficient	13	0	0	0
	Control	146	—	127	244.3
Pair 2:	Deficient	0	0	0	0
	Control	179	40.4	179	30.8
Pair 3:	Deficient	0	0	0	0
	Control	124	133.6	83	376.4
Pair 4:	Deficient	0	0	—	0
	Control	184	103.0	—	546.3
Pair 5:	Deficient	—	0	0	0
	Control	191	139.0	115	382.5
Mean:	Deficient	3.2	0	0	0
	Control	164.8	104.00	126.0	316.06

reached by the deficient animals. Their livers contained no detectable vitamin A, and plasma levels were extremely low when compared with the levels in control animals. The control animals in Experiments I and II and those in group 4 in Experiments III and IV were entirely normal throughout the experimental period.

The skin.—This was studied in 96 out of a total of 106 animals. Samples were obtained from the anterior abdominal wall and the upper parts of fore and hind limbs. The skin of the limbs was studied because of its predisposition to phrynoderma in man. It was, however, found that the incidence and severity of changes in it were not greater than and were similar to those in the other areas. In view of this fact, and also to facilitate comparison with the observations of other workers which were made on abdominal skin, the following account is based mainly on changes found in the anterior abdominal wall. Several sections of the skin of each animal and serial sections in the case of some deficient animals were examined so that individual hair follicles could be followed in their entire course.

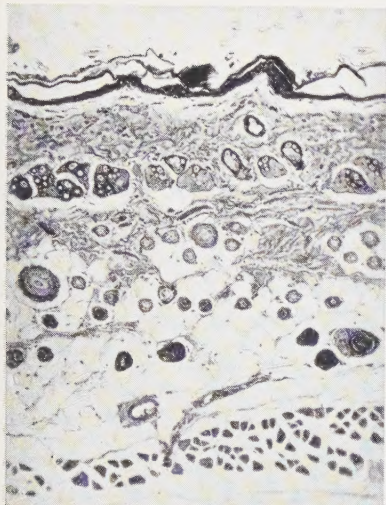


FIG. 5.

FIG. 5.—Abdominal skin of a control rat showing abundance of inter-follicular and subcutaneous fat, numerous normal-looking hair follicles and sebaceous glands and normal epidermis with a loose thin keratin layer. $\times 60$.

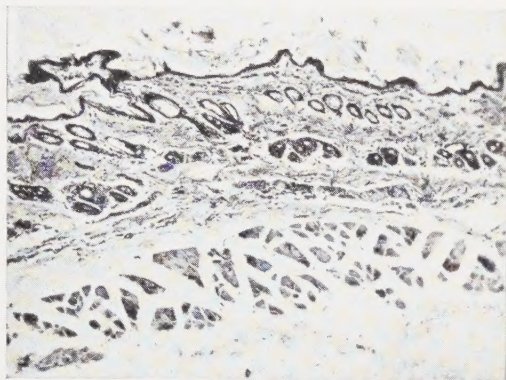


FIG. 6.

FIG. 6.—Abdominal skin of a vitamin A-deficient rat in Experiment I ("acute deficiency") at the end of 10 weeks of deficiency showing complete disappearance of interfollicular and subcutaneous fat, marked atrophy of sebaceous glands and loose surface hyperkeratosis. Near the extreme left can be seen the dilated upper part of a hair follicle containing several loosely-arranged layers of keratin. $\times 60$.

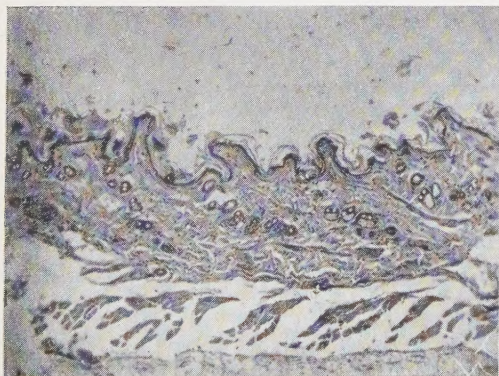


FIG. 7.

FIG. 7.—Abdominal skin of another vitamin A-deficient rat in Experiment I ("acute deficiency") at the end of 10 weeks of deficiency showing features similar to those in Fig. 6, with the addition that there is dilatation of the upper part of the hair follicles causing marked waviness of the surface of the skin. The dilated follicles contain loosely-arranged layers of keratin and their lining epithelium is atrophic. $\times 60$.

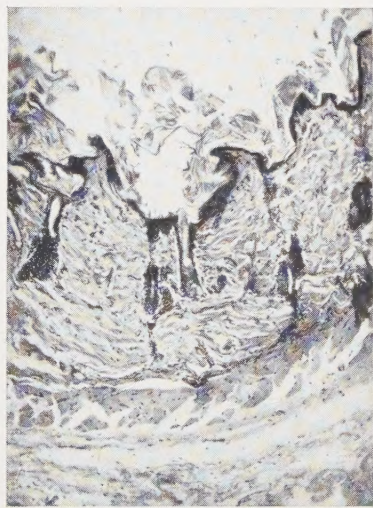


FIG. 8.

FIG. 8.—Abdominal skin of a vitamin A-deficient rat in Experiment II ("chronic deficiency") after 22 weeks of deficiency, showing severe dilatation of the upper half of hair follicles with excessive deposition of loose lamellae of keratin both on the surface and within the dilated follicles. There is also complete disappearance of subcutaneous fat and sebaceous glands. $\times 60$.

Experiment I (acute deficiency of vitamin A) : In this experiment all animals were killed after 10 weeks of deficiency. The skin of the control animals at this time showed normal histological features, which were indistinguishable from those of animals of the same age and sex receiving a complete stock diet (Figs. 5 and 9). The basal and Malpighian layers of the epidermis were one to three layers deep, consisting mostly of flattened cells. There was a distinct stratum

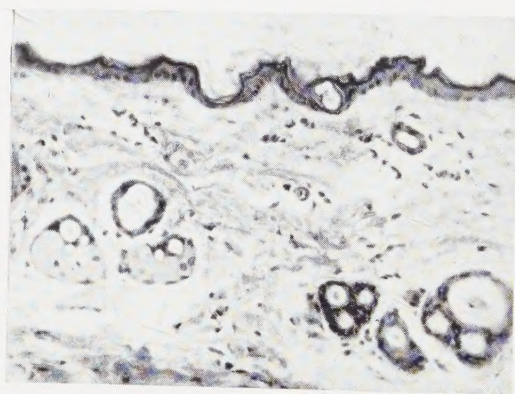


FIG. 9.

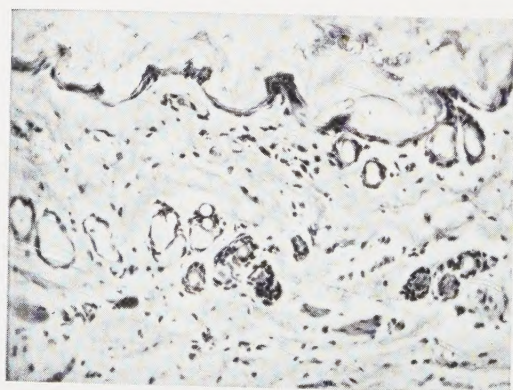


FIG. 10.

FIG. 9.—Abdominal skin of a control rat showing normal epidermis which consists of 1 to 3 layers of stratum Malpighii, thin granulosum, indistinct lucidum and thin corneum. The sebaceous glands and hair follicles appear normal. $\times 167$.

FIG. 10.—Abdominal skin of a vitamin A-deficient rat in Experiment I ("acute deficiency") after 10 weeks of deficiency showing marked atrophy of transitional layers of the epidermis, loose surface hyperkeratosis and disintegration of sebaceous glands. $\times 167$.

granulosum, consisting of one layer of cells. The stratum lucidum was quite prominent in places and indistinct in others. The stratum corneum was thin and somewhat loose. The boundary between the epidermis and cutis was even, no rete pegs being present. The structures of the corium appeared normal. The

hair follicles and sebaceous glands were numerous and closely packed. The follicles were set obliquely and opened on the surface by a slight expansion of their upper ends, thus giving a gentle, wavy appearance to the skin surface. The hair roots reached down to the subcutaneous fat depots. The interfollicular and subcutaneous fat was abundant, being bounded on its deep aspect by a well-developed muscular layer.

The skin of the deficient animals showed a uniformly abnormal picture, although the degree of severity of the individual abnormalities varied in different animals. There was a marked reduction in the thickness of the skin, to a large extent due to an almost complete disappearance of the fat depots, with the result that the corium lay in direct contact with the muscle layer (Figs. 6 to 8). There was a variable degree of atrophy of basal and Malpighian layers of the epidermis, which were reduced in the severest cases to a single layer of greatly flattened cells (Figs. 9 and 10). The stratum granulosum was less distinct, disappearing completely in some places, and the keratohyalin granules were smaller and fewer than in the control animals. The stratum corneum was increased in thickness, the cornified lamellae being loosely arranged. No nuclear remnants were seen in this layer. The stratum lucidum was only occasionally seen.

The upper third of the hair follicles was dilated and its lining epithelium was atrophic. This change was present in all the deficient animals, being mild in about half of them and moderately severe in the rest. The dilated upper parts of the follicles contained, in addition to apparently normal shafts of hair, several loosely-arranged layers of keratin. The follicular dilatation produced marked waviness of the surface of the skin, giving a papillated appearance to the corium (Fig. 7). In some places the dilated upper parts of several adjacent follicles coalesced to form large craters in which numerous hair shafts and layers of keratin could be seen. The epithelial sheaths of the lower two-thirds of the follicles showed no changes. There was a definite reduction in the number of sebaceous glands and many of the remaining glands were in different stages of disintegration, exhibiting dilatation of acini with pyknotic nuclei (Figs. 9 and 10). The corium itself showed no definite changes. The connective-tissue sheaths of hair follicles appeared normal and no perifollicular cellular infiltration was noted.

Experiment II (chronic deficiency of vitamin A): The animals in this experiment were maintained for a period of about 24 weeks, during which time they received supplements of vitamin A at three different intervals—the 9th, 12th and 18th weeks of deficiency. After the last dose the deficient animals were maintained until they were again severely depleted, and were then killed together with their pair-fed controls. Each dose of vitamin A was followed by a prompt, but temporary, improvement in the growth, ocular lesions and general condition of the deficient animals. Microscopically the skin of the control

animals showed no abnormalities, and was similar to that of the control animals in Experiment I. The skin of the deficient animals showed the same pattern of change as in Experiment I. The individual abnormalities were slightly more severe in this experiment, although they were not as severe as was expected after such a prolonged experimental period. Disappearance of interfollicular and subcutaneous fat was complete in all deficient animals, with marked reduction in the thickness of the skin. Atrophy of the epidermis was slightly more marked, as was the surface hyperkeratosis. Dilatation and hyperkeratosis of the upper third of the hair follicle with atrophy of lining epithelium were present in all animals, in two of which the upper half of the follicles was markedly dilated, with atrophic changes in the epithelial lining of the lower half also present (Fig. 8). The changes in sebaceous glands were of the same order of severity as in Experiment I. In none of these experiments were any infections of the skin noted.

Experiments III and IV (partial deficiency of vitamin A) : These experiments were designed to ascertain whether the changes produced in Experiment I, in which rats were maintained on a diet totally devoid of vitamin A up to the stage of complete deprivation, could be modified by maintaining them on sub-minimal amounts of vitamin A. They were planned because naturally occurring deficiency in man is likely to be partial rather than complete. Adolescent rats were used in Experiment III because of the clinical observation that the incidence of phrynoderma is much higher in adolescents than in other age-groups. In both experiments it was found that the skin changes, particularly the follicular change, were not appreciably different from those in Experiment I. In both experiments the animals in group 1 which received no vitamin A and which were therefore comparable with those in Experiment I behaved in a similar way to them in their clinical course and structural changes in the skin and other organs. In the partially deficient groups 2 and 3, although the same type of change was observed, the changes were milder at any given time and later in onset than in group 1. Even in those animals maintained for as long as 14 weeks, the cutaneous changes were of the same type and severity as those in group 1 and Experiment I. The changes found in the adolescent rats in Experiment III were in general milder than those in Experiment IV. The animals in group 4 showed no cutaneous abnormalities, showing that the amount of vitamin A given was sufficient to protect their skin.

DEFICIENCY OF ESSENTIAL FATTY ACIDS.

Experimental Procedure (Experiment V).

Animals.—Twenty-six weanling albino rats, 21 days old, were divided into two groups each of 13 deficient and 13 control animals, littermates being distributed equally between the groups. Each group contained 8 males and 5

emales. They were kept in individual cages with raised mesh floors in a heated room at a constant temperature of 72° F.

Diets and supplements.—The following vitamin-free basal diets were fed to the deficient and control groups :

Composition of diets.

	Deficient (parts %).	Control (parts %).
Sucrose	75	65
Casein (fat- and vitamin-free)	20	20
Arachis oil	—	10
Salt mixture (Hegsted <i>et al.</i> , 1941)	5	5

As the calorie values of the two diets were different, 1 g. of deficient diet yielding about 3·8 cal. and 1 g. of control diet 4·3 cal., in the paired feeding the amount of food given to the control animals was proportionately reduced in order to supply the same number of calories. All animals received, daily by mouth, the water-soluble vitamin mixture already mentioned. One thousand i.u. of vitamin A and 2·5 mg. of α -tocopherol were given by mouth at weekly intervals to all animals. In order to avoid fats completely, pure crystalline vitamin A acetate (Roche) and α -tocopherol acetate were dissolved separately in absolute alcohol and two drops of each containing the requisite amounts of the vitamins were added to the water-soluble vitamin supplement just before it was administered. The alcoholic solutions were freshly prepared every three weeks, and every week the vitamin A content of the solution was estimated by the Carr-Price reaction before administration. No vitamin D was given ; its need in the presence of a complete salt mixture cannot be demonstrated in the rat (Brown and Sturtevant, 1949).

Methods.—The methods followed in this experiment for studying the clinical course and structural changes were the same as those used in the experiments on vitamin A.

Results.

Judged by the various criteria of clinical condition, the deficiency process in this experiment was found to be a slowly progressive one, unlike that in deficiency of vitamin A. The deficiency was characterized by failure of growth, lesions of the paws and mucocutaneous junctions, and increased consumption of food and water. The changes in the dorsa of the paws consisted of erythema, oedema, scaliness and dryness. Scaly changes in the ears appeared more consistently than in the tail towards the later stages of deficiency. The details of the clinical features and structural changes in several organs will be described separately elsewhere (Ramalingaswami and Sinclair, 1952). In this section only

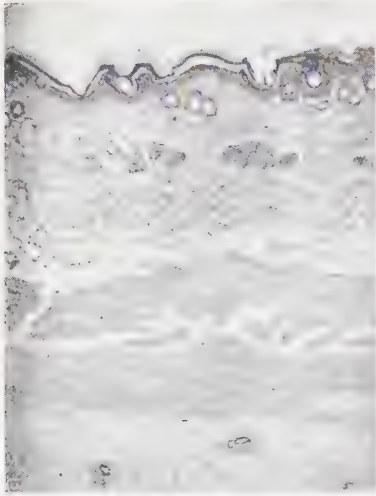


FIG. 11.

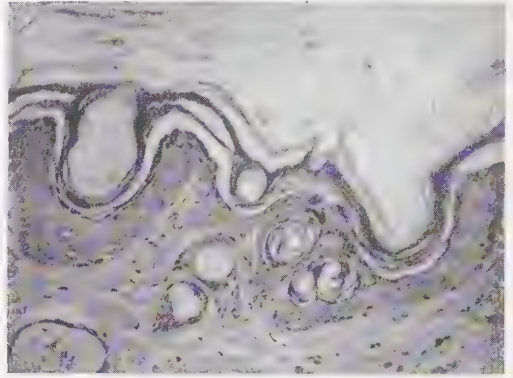


FIG. 12.

FIG. 11.—Abdominal skin of a fat-deficient rat (Experiment V) after 23 weeks of deficiency. There is a slight reduction of subcutaneous fat, increase in thickness of transitional layers and of the stratum corneum of the epidermis. The stratum corneum is compact and dips down into the openings of hair follicles. Note also the prominent and enlarged sebaceous glands. $\times 52$.

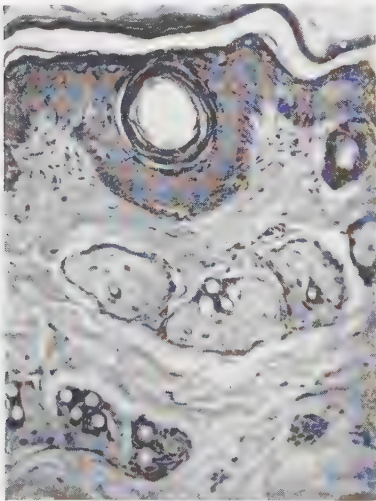


FIG. 13.

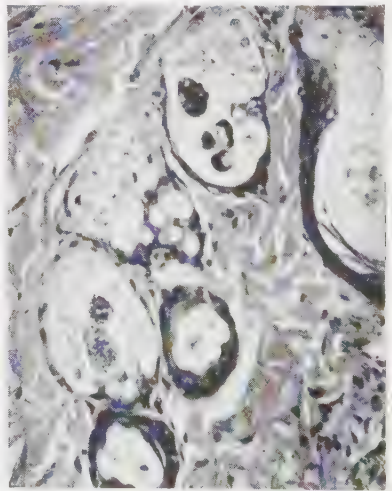


FIG. 14.

FIGS. 12 and 13.—Abdominal skins of fat-deficient rats (Experiment V) after 23 weeks of deficiency, showing plugging of the openings of hair follicles with dense concentrically arranged layers of keratin. There is also marked acanthosis of the epithelium lining the follicular openings which is slightly more severe than in the rest of the epidermis. Slight increase in connective-tissue cell nuclei underneath the epidermis can be seen in the region of follicular openings. Greatly enlarged and plump sebaceous glands can be seen. $\times 167$.

FIG. 14.—Abdominal skin of a fat-deficient rat (Experiment V) after 24 weeks of deficiency showing granular basophilic material in the enlarged sebaceous glands. $\times 200$.

the changes in the skin will be described. The following account is based on examination of all 26 animals which were killed between the 24th and 30th weeks of deficiency.

The skin. The abdominal skin of the control animals showed no abnormalities, and was similar to that of the control animals in the experiments upon deficiency of vitamin A. The skin of the deficient animals, on the other hand, showed definite and uniformly abnormal features, which differed from those seen in deficiency of vitamin A in almost every respect (Figs. 11 to 14). Although there was a slight reduction in the amount of interfollicular and subcutaneous fat in comparison with the control animals, it was never so complete as in deficiency of vitamin A. In all animals a fairly well-defined layer of fat cells was present separating the corium from the muscular layer. This finding was remarkable, considering the fact that the animals had been completely deprived of dietary fat for a period of six months. There was a marked increase in the thickness of surface epithelium, which consisted of from 4 to 8 layers of cells, the increase being both in the stratum Malpighii and granulosum (Figs. 12 and 13). There was no definite increase in the mitotic figures of the basal layer and no rete peg formation. The granulosum was composed of 3 or 4 layers of cells instead of the normal single flattened layer, and its cells were packed with numerous irregular densely-staining granules. The granules were small and rounded in the deeper layers, but assumed large ovoid shapes in the superficial layers. The stratum corneum was markedly increased in thickness. The keratin layers were closely packed and adherent, unlike the loose lamellar arrangement in deficiency of vitamin A. No nuclear remnants were seen in the corneum. The hyperplasia of surface epithelium increased in severity in the region of the openings of hair follicles with the result that the Malpighian and granular layers of their lining epithelium were markedly increased in thickness. The stratum corneum was also increased in thickness and the keratin layers were found to invest closely the emerging hair shafts in a concentric fashion and to plug the openings of hair follicles (Figs. 12 and 13). This acanthosis and hyperkeratosis of the epithelium lining the follicular openings extended only for a short distance down the main body of the follicle itself, in severe cases the uppermost quarter of the follicle being involved. In no case did the process reach as far down as the opening of the sebaceous gland into the follicle and the remaining part of the follicle appeared quite normal. A striking feature in the corium was that the sebaceous glands remained intact and were in fact hypertrophied: the acini of the glands were more numerous and larger than those of the control animals (Figs. 11, 12 and 13). In addition, in all the male deficient animals a fine granular basophilic material was found in the sebaceous glands (Fig. 14); this was found in places where the acini of the glands had disappeared and seemed to be a degeneration product of the acini. In the superficial part of the corium, immediately underneath the basal layer

of the epidermis, a marked increase and distension of the capillaries and a mild mononuclear cellular infiltration were observed in places, not specifically in the region of the follicular openings. The rest of the corium showed no definite changes. The histological changes in the skin of the paws and ears were found to be generally similar to those in the abdominal wall, with the exception that the follicular plugging was much less marked. In the ears, in addition to these features, there was acute bending and distortion of the cartilage with marked dilatation of the subcutaneous blood-vessels.

The exact pathogenesis of these striking changes in the epidermis of various regions is not clear. It was not possible in this investigation to decide whether the epidermal changes were a consequence of disturbed circulation in the corium, or whether the vascular changes observed in the corium were the result of a primary epidermal abnormality.

DEFICIENCY OF PYRIDOXINE.

The histological changes in the skin of the rat in pyridoxine deficiency were described in detail by Sullivan and Nicholls (1940) and by Antopol and Unna (1942). In addition to changes in the paws, both these groups of workers studied changes in the skin of the trunk and reported atrophy of hair follicles and sebaceous glands in late stages of deficiency. Since weanling rats were used by both groups of workers, we investigated in Experiment VI the effect of deficiency of pyridoxine on cutaneous structure of older rats. Twenty-four albino rats, 11 weeks old, were divided into two groups of 12 deficient and 12 control animals. They were kept on the experimental regimen for about 20 weeks. The histological changes in the abdominal skin of the deficient animals at the end of this period consisted of atrophy of the epidermis, hair follicles and sebaceous glands, with loose hyperkeratosis and loss of subcutaneous fat. The higher age of the animals used in this experiment, therefore, seems to have had no influence in modifying the changes described by the above authors. Since they bear no resemblance to the lesion in phrynoderma, details of this experiment will be omitted. The changes in the dorsal aspect of the skin of the paws were superficially similar to those in deficiency of fat, and consisted of oedema and vascular engorgement of the corium associated with marked acanthosis and hyperkeratosis of the epidermis.

DISCUSSION.

Before discussing the results of this work it is essential to define clearly the histological criteria that should determine the identity of the experimentally produced lesion in the rat with that in phrynoderma. Fortunately, excellent histological descriptions of the skin in phrynoderma have been given by Frazier and Hu (1931), Loewenthal (1933) and Radhakrishna Rao (1937). First, all

authors are agreed that the fundamental lesion in phrynoderma is plugging of the openings of hair follicles by dense masses of keratin. Thus, Loewenthal (1933) finds that "the histological features of this condition are absolutely typical, and never vary more than can be explained by the degree of severity of the condition. . . . The mouth of the follicle is completely sealed by a dense mass of horny tissue, the surface of which is flush with the horny layer of the surrounding skin." Secondly, all these authors find that, associated with hyperkeratosis of follicular openings, a generalized surface hyperkeratosis and acanthosis of the epidermis which become more marked as the follicle is approached are also present. Other features have been reported, such as atrophy of sebaceous glands, mononuclear and lymphoid cell infiltration in the perifollicular area, and intrafollicular abscess formation: but some of these must be regarded as secondary to the above changes and others have not been consistently observed. Changes in the ducts of the sweat glands have also been described, but as these glands are rudimentary in the rat this feature cannot be used as a criterion. It is clear, therefore, that only the first two features—namely, plugging of the opening of the hair follicles with dense masses of keratin and hyperplasia of their lining epithelium, together with generalized surface hyperkeratosis and acanthosis of the epidermis—can be regarded as characteristic features of phrynoderma.

In attempting to compare these changes in the human skin directly with those produced experimentally in the rat, the similarities and differences in the normal architecture of the skin of the two species have to be considered. Although the skin of the rat is similar in many respects to that in man, several differences exist. In the rat the coil glands are rudimentary, the epidermis is composed of fewer cell layers, and, what is most important in the present context, the hairs on the trunk and extremities are much more numerous than in man. Whereas the hair follicles in these areas are separate and discrete in man, they are so much more numerous and closely set in the rat that this difference is bound to have some influence on the development of a lesion resembling phrynoderma. Obviously no exact counterpart can be expected in the rat.

It is, therefore, surprising to find the close similarity of the changes found in deficiency of essential fatty acids in the rat to those which are described above as characteristic of phrynoderma. In rats deficient in fat there is acanthosis and surface hyperkeratosis of the epidermis, which increase in severity in the region of the openings of hair follicles. The lining epithelium of follicular openings also shows changes similar to those of the surface epithelium. The dense compact keratin layers closely invest the emerging hair shaft, plugging the follicular opening. The keratotic plugging of the follicular openings and the increase in thickness of their lining epithelium are factors which are most conducive to elevation of the lesion above the surface, and this elevation can in fact be seen in the figures (Figs. 12 and 13).

In spite of this striking similarity between the follicular changes in deficiency of fat in the rat and those in phrynoderma, a certain amount of uneasiness will still be felt regarding the extent of follicular hyperkeratosis in the two conditions. In experimental deficiency of fat the hyperkeratosis and plugging are confined to the openings of hair follicles, and do not extend for any appreciable distance down the main body of the follicle. Although in their original descriptions Frazier and Hu (1931), Loewenthal (1933) and Radhakrishna Rao (1937) described involvement of the mouths of hair follicles as characteristic and Loewenthal (1933) specifically stated that "the plug occurs in the form of an inverted pear, the lowest part of which is superficial to the entrance of the sebaceous duct," yet in some of the illustrations of these and other authors the impression has been gained that the follicular plug in phrynoderma extends deeper down the follicle than that found in the skin of the fat-deficient rat. This difference, however, is probably not significant and to be expected when dealing with two different species. It is also possible that, given a longer time, or in combination with other deficiencies such as those of calories, vitamin A, and other nutrients, the follicular plugs in deficiency of fat would extend more deeply into the follicle. Another difference between the human and experimental lesions is in the state of the sebaceous glands, which are hypertrophied in deficiency of fat and usually atrophied in phrynoderma. Undue significance cannot be attached to this as, presumably, the hypertrophy is only an earlier stage of a degenerative process caused by obstruction to the outflow of sebum by the keratotic plugs.

There is thus no fundamental difference between the follicular lesion in fat-deficiency in the rat and that in phrynoderma in man. It was not possible, in this investigation, to decide where the change first starts—whether in the lining epithelium of the follicular openings, or in the surface epidermis. But apparently this is not of importance, since all accounts of phrynoderma mention generalized surface hyperkeratosis and acanthosis of the epidermis, and it appears that these features are as much a part of phrynoderma as are the follicular changes. Further, in pityriasis rubra pilaris, which is very similar to phrynoderma histologically but which cannot be mistaken for it clinically, diffuse hyperkeratosis of surface epithelium in addition to follicular hyperkeratosis is a characteristic feature (MacLeod and Muende, 1940).

In deficiency of vitamin A in the rat, on the other hand, the changes consisted of dilatation and loose hyperkeratosis of the upper third of the hair follicles, atrophy of surface epithelium with loose hyperkeratosis, atrophy of sebaceous glands and almost complete loss of subcutaneous fat. Although a definite follicular abnormality was produced which superficially appears to resemble the lesion in phrynoderma, on closer examination several fundamental differences are found to exist. Instead of the generalized acanthosis and compact hyperkeratosis of the surface epithelium in phrynoderma, there is atrophy with loose

hyperkeratosis. Instead of the dense keratotic plugging of the follicular openings and hyperplasia of their lining epithelium in phrynoderma, there is wide dilatation of the upper third of hair follicles with atrophic epithelium and loose hyperkeratosis. The follicular dilatation and atrophy of lining epithelium and loose hyperkeratosis in deficiency of vitamin A in the rat can only result in the formation of craters rather than papules in the skin (Figs. 7 and 8). It was, however, thought that by prolonging the period of deficiency sufficient time would be allowed for more extensive deposition of keratin, thus resulting in the formation of a dense intrafollicular plug protruding above the surface. In Experiment II, therefore, rats were maintained for over 24 weeks on a diet deficient in vitamin A by intermittent supplementation with vitamin A. It was also thought that the small amounts of vitamin A given might result in reparative proliferation of lining epithelium of follicular openings which would help in the elevation of the plug. But this procedure resulted in slightly more severe dilatation of the hair follicles, with formation of deeper craters, the keratotic layers still remaining loose and the follicular epithelium becoming more severely atrophied. The influence of higher age and partial deficiency were next investigated in Experiments III and IV, and again the follicular lesions were not altered in any way. Thus it is clear that deficiency of vitamin A in rats results in follicular lesions that do not resemble those in phrynoderma.

The changes found in deficiency of pyridoxine in the rat bear no resemblance to those in phrynoderma.

It is interesting to note that, although the follicular changes in deficiency of vitamin A in the rat do not resemble those in phrynoderma, they are closely similar to the histological changes described by Radhakrishna Rao (1937b) in persons with keratomalacia who did not show papular skin lesions clinically, and in whom he described epithelial atrophy, follicular dilatation and surface hyperkeratosis. He believed that the patients were suffering from a pure deficiency of vitamin A and interpreted the findings as being early stages of phrynoderma. In view of the similarity of these changes with those found in uncomplicated deficiency of vitamin A in the rat in the present series of experiments, it is most likely that the changes described by Rao were in fact the result of deficiency of vitamin A in man. But it is difficult to accept his suggestion that they represent an early stage of phrynoderma. As already stated, it was not possible to modify the nature of these changes by prolonging the deficiency period, by inducing partial deficiency or by using adolescent rats.

The implications of these studies in rats when tentatively extended to man are that deficiency of essential fatty acids might be important in the aetiology of phrynoderma and that deficiency of vitamin A does not play any direct part in its causation. The vast amount of clinical literature on phrynoderma is not incompatible with this hypothesis. Cures claimed for deficiency of vitamin A from treatment of phrynoderma with fish-liver oils are probably due to the

unsaturated fatty acids in the fish oils. Support for this hypothesis can be claimed from the results of nutritional surveys of Aykroyd and Rajagopal (1936), who were, in fact, the first to suggest that "phrynoderma may possibly be due to deficiency of fat in the diet, which prevents lubrication of the skin." More recently, Gopalan (1947) and Menon *et al.* (1950) successfully treated several cases of phrynoderma with vegetable oils alone. The latter workers have also found a lowering of the degree of unsaturation of plasma lipids in cases of phrynoderma which could be reversed on treatment with sesame oil. Thus, phrynoderma seems to have started on the same journey as infantile eczema nearly two decades ago.

In spite of the experimental and clinical evidence in support of the hypothesis of deficiency of essential fatty acids, it should be remembered that the cutaneous changes in deficiency of fat in the rat were produced after six months of complete deprivation of fat. Presumably such complete absence of fat for a prolonged period never occurs naturally in man. But, on the other hand, it is possible that with the extremely low fat diets such as are consumed in South India, a deficiency of these acids can arise in man. The work of Hansen and his colleagues (1947) has already demonstrated the beneficial effects of these fatty acids in the treatment of intractable cases of infantile eczema. It may well be that the essential fatty acids will prove useful not only in the treatment of phrynoderma, but also in the whole range of affections characterised by hyperkeratization of the epidermis and mouths of hair follicles. In the latter the beneficial effects, if any, may be brought about by pharmacological action rather than by correction of a primary dietary deficiency.

SUMMARY AND CONCLUSIONS.

1. Following a review of the literature on the nutritional aspects of follicular hyperkeratosis, it was found that deficiencies of vitamin A, essential fatty acids and pyridoxine urgently required investigation, being possible factors in the aetiology of phrynoderma in man. In a series of six experiments involving the use of 156 rats, deficiencies of these nutrients were induced individually.
2. In deficiency of essential fatty acids the changes in the skin were found to be closely similar to those in phrynoderma.
3. In deficiency of vitamin A the skin changes bear only a slight resemblance to those in phrynoderma. They could not be influenced appreciably by prolonging the period of deficiency, or by producing states of partial deficiency, or by using adolescent rats.
4. In deficiency of pyridoxine, also, the skin changes were different from those in phrynoderma.
5. On the basis of this experimental evidence, it is suggested that deficiency of essential fatty acids may be the cause of phrynoderma in man. The clinical literature on phrynoderma is not incompatible with this hypothesis.

We are deeply indebted to Mr. E. H. Leach, University Laboratory of Physiology, Oxford, for his help in the preparation of microphotographs and for advice at all times in histological methods. Our thanks are due to Miss E. Oehlmann for estimations of vitamin A. and to Miss B. Yeates for secretarial assistance. It is a pleasure to acknowledge the constant help throughout this work of Miss J. Buxton.

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ROYAL SOCIETY OF MEDICINE.

SECTION OF DERMATOLOGY.

President—Dr. G. B. DOWLING.

15 May 1952.

Acute Disseminated Lupus Erythematosus (Now Quiescent on ACTH).—

Dr. DENIS SHARVILL (for Dr. SYDNEY THOMSON.)

Miss M. L—, aged 22, secretary.

Admitted to King's College Hospital Unit, Dulwich Hospital, 24 April 1952, complaining of rash on face, hands and legs and of inability to eat or drink.

History of present illness.—Was perfectly well until the end of March (a week-end of snow) when she felt cold and sat by the fire. This brought on redness of the legs and fingers, which she thought were chilblains. She applied elastoplast to the fingers, and when she removed it they were raw and bleeding. Ten days later she felt giddy and lethargic and spent a week in bed; her doctor diagnosed chilblains and food-poisoning and gave five injections of penicillin. A week before admission a rash appeared on the face and got rapidly worse. The fingers also rapidly deteriorated and bled profusely, and she noticed pain and swelling of the right knee. Her mouth became very sore so that she could neither eat nor drink, although she felt hungry. She had a slightly sore throat. She felt quite well in herself. She has not taken sulphonamides or any other drugs.

Previous history.—No major illnesses. No rheumatism. 1947: Chest skiagram normal. 1948: Measles. 1951: Went hiking and got sunburned. The skin took three months to return to normal, but she attaches no significance to this.

Family history.—Nothing of note.

On examination.—A symmetrical erythematous rash on the face, forehead, ears, shoulders, upper arms, backs of hands, fingers, shins and toes. It was a vivid purple red, most intense on the face and fingers and very sharply demarcated.

On the face the batswing area was involved. There was no scaling or plugging. The palate had erythematous lesions, and haemorrhagic crusts were present on the lips.

All the fingers were severely affected, the extensor surfaces more than the flexor, distally more than proximally. At the nail-folds and over the interphalangeal joints there was erosion of the epidermis and profuse bleeding.

A few purpuric macules were present on the trunk. The shins showed sheeted erythema. The toes showed changes similar to the fingers but of lesser degree.

On general examination.—She was alert and co-operative but looked desperately ill. The temperature and pulse-rate were raised. The tongue was very dry. During the previous week the temperature had varied between 100° and 102° F.

No abnormality was found in the cardiovascular system except a soft systolic murmur at the apex. Blood pressure 120/45. The respiratory system appeared normal. The spleen and liver were not felt. There was no lymph-gland enlargement.

26 April (Dr. Samuel Oram): There is no real evidence of cardiac involvement on clinical grounds . . . the soft systolic murmur could be accounted for by fever and tachycardia.

9 May (Mr. R. P. Crick): When first seen on 29 April a few patches of white exudate were visible ophthalmoscopically lying superficially in the retina, close to and some overlapping the larger branches of the retinal vessels near the optic disc. Though circumscribed their appearance suggested that they were of recent origin. No other fundus abnormalities were seen and the visual acuity was unimpaired. To-day only one patch of exudate remains in the left eye.

Special investigations on admission.—Urine: Heavy cloud of albumin. Scanty leucocytes and red cells. Numerous hyaline, cellular and granular casts. Sterile after eighteen hours' culture.

Blood (25 April): R.B.C. 3,500,000; Hb 11.3 g.%. Haematocrit 32 mm./100 mm. Leucocytes 2100/c.mm. Platelets were present in adequate numbers on this date. Blood film: Neutros. 58, lymphos. 39, monos. 3%. Corrected E.S.R. (Wintrobe) 26 mm./hr. E.S.R. (Westergren) 80 mm./hr.

L.E. cells were produced on adding the patient's plasma to her own leucocytes and to normal bone-marrow.

Bone-marrow was not examined initially as the patient was in such discomfort, and since it was thought that it might be dangerous in view of the low white count and bleeding tendency. (On 12 May bone-marrow appeared essentially normal.)

Skin biopsy was not done. Serum proteins (suspect for technical reasons): Total 5.38 g./100 ml. Albumin 3.41 g./100 ml. Globulin 1.97 g./100 ml. (Chromatography showed reduced albumin and increased α_2 globulin.) Blood urea: 40 mg./100 ml. Throat swabs: No haemolytic streptococci. Twenty-four-hour urine showed no abnormal porphyrins. 17-ketosteroids normal.

Chest skiagram normal. Serum proteins repeated 15 May. Total 5.68 g./100 ml. Albumin 3.08 g./100 ml. Globulin 2.60 g./100 ml. A.G. ratio 1.18:1.

Coombs test negative.

Treatment and progress.—The hands were kept constantly soaked in wet dressings of hydrarg. perchlor. 1:2000 in normal saline which gave great relief; sepsis did not appear.

ACTH 40 mg. eight-hourly was started on 26 April, and next day she felt vastly better, could eat and drink without discomfort, and the temperature had fallen to normal.

By 28 April the erythema was visibly fading. W.B.C. 3300. The hands were no longer bleeding. On 29 April ACTH was reduced to 80 mg. daily. On 2 May the face was very much paler and beginning to scale. The hands were painless. She talked of getting up and going home.

3 May: ACTH 60 mg. daily.

7 May: ACTH 40 mg. daily.

On 8 May the temperature rose. A painless subcuticular whitlow appeared and was evacuated. ACTH raised to 60 mg. daily next day.

13 May: Temperature settled. Still well.

Comment—The patient's serum proteins in the first instance were normal, but the result was suspect. Clinically there was no evidence of cardiac involvement, but in the electrocardiogram changes in the T waves indicated involvement of the myocardium. The clinical response to treatment was dramatic; there was subjective improvement within eight or ten hours of the first injection and objective change in the erythema within twenty-four hours. I do not know what mepacrine does in acute disseminated lupus erythematosus. The sedimentation rate has remained very high. The white count has gone up from 2000, when she started, to 3200 in ten days, and 4000 to-day.

Dr. F. RAY BETTLEY: It has been asked whether mepacrine has any effect in the acute case. The only such case I have treated with mepacrine, a woman who had all the objective signs of acute lupus erythematosus without a great deal of systemic disturbance responded at once: she relapsed when we ceased to give the drug, and there was a further response on re-starting. Both responses and relapses occurred within about twenty-four hours. The dose was 100 mg. a day.

Dr. L. FORMAN: A case in Guy's Hospital of subacute disseminated lupus erythematosus with a slight temperature has responded very satisfactorily to mepacrine. The erythema has faded and she has put on weight. Hargraves's cells present in large number in bone marrow have now become difficult to demonstrate. Dr. R. Waterfield has watched the formation of the Hargraves cell under the phase-contrast microscope. He saw the polymorphonuclear cells advance on the bodies and surround them, the protoplasm of the phagocytic cell flowing round the lupus erythematosus body. However, this attachment may not be permanent. After a time, from a few minutes to two hours,

the leucocytes may slip off again. Thus a fixed and stained smear might not reveal the lupus erythematosus cells.

Dr. H. R. VICKERS : I would like to raise a note of warning. My colleague, Dr. I. B. Sneddon of Sheffield, had under his care a case similar to this. She responded dramatically to ACTH and was to have been demonstrated at the January meeting. Her sedimentation rate remained raised, and a few days before she was to be demonstrated she relapsed. She rapidly went downhill and died within about ten days of the relapse in spite of ACTH and cortisone in large doses given intravenously. I think in this patient, since the sedimentation rate is still very high, the chances are that she will relapse and probably die. The case I have mentioned is being prepared for publication by Dr. R. H. Martin, the Registrar in the Department.

Dr. SHARVILL, in reply : There is no evidence of tuberculosis. The chest skiagram is normal, and no acid-fast bacilli have been found in the sputum or urine.

I hope later to be able to try the effect of mepacrine, when the condition is more stable, or perhaps that of oral cortisone. I do not know whether paludrine has any effect : I see no reason why it should—it is not chemically related to mepacrine.

I do not think that dissemination was caused by penicillin ; systemic illness was present before it was given.

When we reduced the dose of ACTH to 40 mg. a day her temperature rose, settling on a subsequently increased dose. This may, however, have been due to the presence of a subcuticular whitlow.

Addenda : 18 July. —Seven weeks ago ACTH was reduced to 30 mg. daily and stopped five weeks ago. Since then she has had mepacrine 100 mg. daily for two weeks, then 100 mg. twice a week. She has remained very well—she says that she feels better than when on ACTH—and there has been no rise of temperature or other ill-effect. The B.S.R. is now 30 mm. hour (Westergren). The skin appears normal. The E.C.G. has become normal. She has been discharged from hospital and is up and about.

12 Sept.—She is now back at work. No treatment has been given for the past six weeks.

Two Cases of Angioma Serpiginosum.—Dr. L. A. M. B. MUSSO (for Dr. G. B. DOWLING).

This condition, originally described by Hutchinson (1889–90) under the title of “A Peculiar Form of Serpiginous and Infective Naevoid Disease,” was given its present name by Radcliffe-Crocker in 1893.

Case 1.—S. G—, female aged 13.

The red spots, first noticed at the age of 6 years on the middle of the inner side of the left thigh, increased in number until about twelve months ago and not since. On the right thigh similar spots noticed two years ago. They are symptomless, and unaffected by the weather. The patient is unable to state the mode of spread of the lesions, and none seem to have disappeared.

On examination.—An area approximately 12.5 cm. $\times$ 11.5 cm., on the middle of the left thigh on the anterior and antero-medial aspects, consisting of purplish red, pin-point size, flat angiomatous lesions which are either discrete, or in groups of irregular shape, or have some tendency to be arranged in linear, or arc-like fashion. They are not emptied by pressure, and there is no associated erythema (see Fig. 1).

A very small area on the front and upper aspects of the right thigh consisting of a few discrete and one group of the same angiomatous lesions is present. The skin concerned shows no other abnormalities, and no other vascular naevi were found on examination of the rest of the skin.

Case 2.—I. B—, female, aged 11.

First noticed red spots at the age of 5 on the back of the right leg, then at the age of 9 on the back of the right thigh, those on the right buttock being noticed at St. John's Hospital in June 1951. The spots are still spreading on the right thigh and right buttock. No symptoms, but the spots are more prominent in winter. The mode of spread of the spots is unknown, and it is considered that none has disappeared.

On examination.—Over the right tendo Achillis, and on the back of the right calf in an area 20 cm. $\times$ 5 cm. approximately, there is a partly reticulate network of red, pin-point size, flat angiomatous lesions with surrounding erythema. On the centre of

the back of the right thigh there is an area of 12.5 cm. 12.5 cm. approximately, with a few outlying, discrete smaller lesions on the lower inner aspect, of mauve-coloured, flat pin-point angiomatous spots, mostly discrete, though some are in groups and one small ring is visible. On the right buttock there is an area of angiomatous lesions, similar to though generally smaller than on the right thigh, and without ring formation.

The spots do not disappear completely on pressure from any area, except on right calf.

Except for livedo racemosa on the lower extremities, which is worse in winter, the skin concerned shows no further abnormalities, and no other vascular naevi were found on examination.

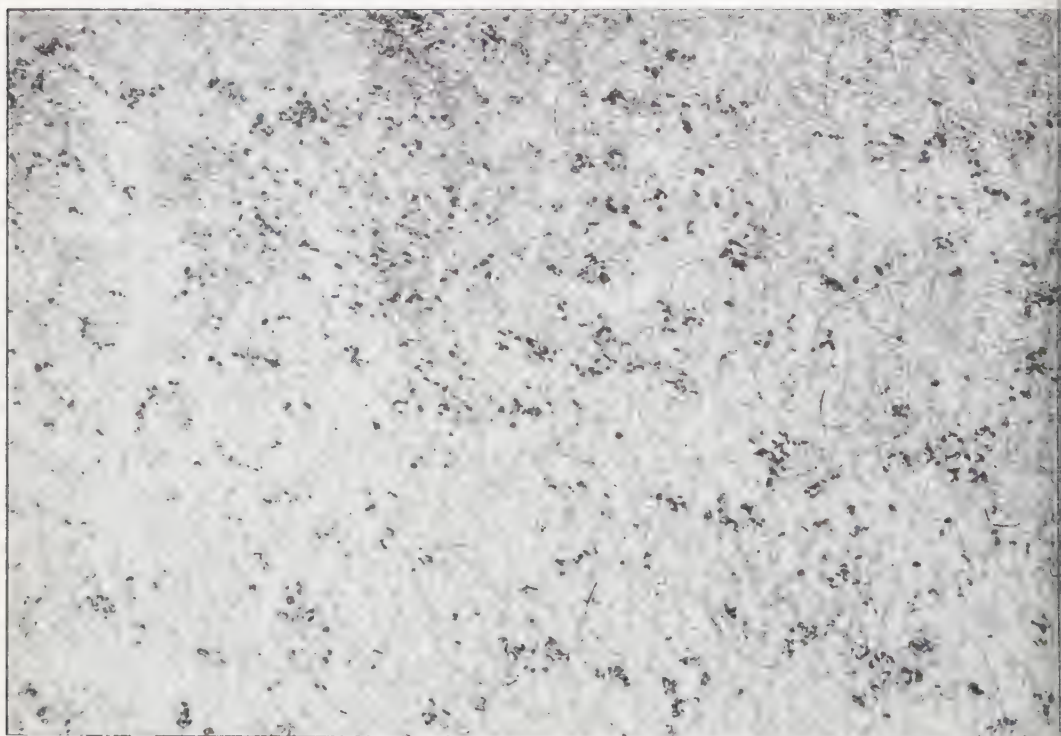


FIG. 1 (Case 1).—Photograph of skin. $\times 2$. The arrangement of the minute spots on the left thigh is well shown, viz. discrete, irregularly-shaped groups, or with some tendency to are-like formation.

Comment.—These two cases are similar, though of different degree, and the following extracts will show that they fit in with the second and fourth cases described by Hutchinson, for only one or two rings were present in each patient :

Essentially in Hutchinson's first case (1889-90), a very slightly marked port-wine stain was observed at the back of the arm soon after the infant's birth. For years it scarcely spread at all, and then began slowly to advance somewhat peculiarly, appearing as if little satellite spots had been produced which had spread into circles, and, by gradually advancing by infective edges, had coalesced, producing the irregular pattern which is here displayed. The conditions are no ordinary part of naevoid disease. They were extremely superficial, and it was even difficult to be sure whether or not they left any sort of scar behind them. He had, however, no doubt that such was their

tendency, and that in some places a slightly-marked, superficial scar could be demonstrated. The enlarged capillaries could be partly emptied by pressure, but not wholly, and in many places little tufts were distended with deep purple venous blood, which could be pressed out.

In the second case described by Hutchinson (1890-91*a*) in a patient of Dr. Allan Jamieson of Edinburgh, the arrangement of the lesions is in the form of minute puncta, some set closely together so as to form groups, others isolated, some arranged in lines. The individual puncta range in size from the diameter of a small pin, to points scarcely recognizable unless with the aid of a lens; the larger are a dark, the smaller a clear red. In the spaces between the grouped puncta the skin is stained a faint pink. In one situation the puncta are clear and sharp, and have no intermediate staining.

In Hutchinson's fourth case (1891-92), a patient of Mr. Warren Tay, minute dots of deep red, or almost purplish tint, of variable size and very small indeed were closely placed, but, for the most part, discontinuous with each other, and not arranged in rings, or in any other definite kind of grouping. There was no evidence of any retrogressive changes, and not the slightest trace of scar could be detected. In a recent patch the dots were not so closely placed.

Hutchinson stated that a feature of difference in the fourth case from other cases of this malady was the slight tendency to form rings or crescents, which was marked particularly in Dr. Lassar's case cited by Hutchinson (1890-91*b*) and his own first case.

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 HUTCHINSON, J. (1889-90) *Arch. Surg., Lond.*, **1**, Plate I.
 ——— (1890-91*a*) *Ibid.*, **2**, 71.
 ——— (1890-91*b*) *Ibid.*, **2**, 111.
 ——— (1891-92) *Ibid.*, **3**, 166.

THE PRESIDENT: Recently some of us have seen in Germany a patient diagnosed as purpura annularis telangiectodes but without scarring, therefore not a typical example of Majocchi's disease. It was, however, a typical example of the annular or serpiginous form of Hutchinson's disease.

? Reticulocytosis: Case for diagnosis.—DR. A. D. PORTER.

G. H. F—, aged 49, married; no children. Previous occupation, soldier (served in India, Egypt and Turkey).

Complained of "Lumps in skin and difficulty in seeing."

Past history.—Jaundice 1930. Malaria, heat exhaustion, dysentery (? type), diphtheria, shingles, double inguinal hernia.

Family history.—All healthy apparently.

History of present attack.—First noticed painful lumps on soles of feet when serving in the Army in 1945. Fresh nodules soon began to appear elsewhere, especially on the face, neck and shoulders, and have persisted. Although some nodules have disappeared and others become smaller the condition has steadily progressed during the last few years. Pressure on the eyeballs has required surgical intervention on several occasions. Between two and three years ago "spots" appeared on the stomach.

On examination.—A well-developed man whose face is deformed by subcutaneous swellings, some of which press upon the eyeballs and have reduced the palpebral fissures to narrow slits. On palpation the swellings are felt as firm, well-defined nodules lying within the subcutaneous tissue and attached to the skin. They vary in size from a few millimeters to several centimetres in diameter. The nodules are only very slightly tender and can be moved freely over deeper structures, with the exception of certain nodules which appear to be attached to the upper ends of the tibiae and may be of a different nature. In the umbilical and sacral regions are numerous discrete, firm, elongated papules, purplish-red in colour and between 1-10 mm. in length. The skin covering the nodules appears normal. On the palate, near the uvula, there are a few deep red infiltrated lesions. Apart from the condition described, no abnormalities were found except some pyorrhoea.

Investigations.—Blood count : W.B.C. 11,900. Neutros. 57%, lymphos. 31%, monos. 6%, eosinos. 6%. W.R. and Kahn reactions negative.

Skiagrams : Bones (skull, pelvis, knees and chest) normal ; lungs normal. Serum cholesterol normal (167 mg. 100 ml.).

Ophthalmic surgeon's report (Moorfields Hospital).—Vision = $\frac{4}{80}$ with restricted fields. Eyes are structurally normal, discs not pale. Difficult to explain the apparent visual defect.

Biopsy report (Dr. H. Haber).—There is a lobulated tumour replacing the fat tissue to a large extent. The stroma of the tumour is fibrotic and the tumour itself consists of a syncytium of reticulum cells of purple or pale colour. The cytoplasm is abundant, showing granular to foamy appearance. The nucleus is round or oval and vesicular. There are also many bi- and multi-nucleated giant cells demonstrable. Some cells contain up to seven nuclei, all situated in the centre of the cytoplasm as in Dorothy Reed cells. There is also a marked admixture of inflammatory cells consisting of eosinophils, plasma cells, polymorphs, round cells and mast cells. One or two mitotic figures could also be demonstrated.

Discussion.—The many hard, well-defined subcutaneous nodules which are yet attached to the skin make this case unusual. The feel of the nodules suggests that they might be formed largely of fibrous tissue, and this impression is confirmed by microscopic examination, which shows them to consist largely of fibrous tissue and reticulo-endothelial cells. Many of the latter are "foamy" and some contain lipid material. A few multi-nucleated giant cells are present and a mixed cellular infiltrate.

These appearances made three independent histologists diagnose xantho-fibromatosis. While this is perhaps an accurate histological description, it does not conform to the nature of the case clinically, which is certainly not that of any ordinary form of xanthomatosis.

The normal serum cholesterol and the lesions on the palate make one think of the eosinophilic xanthomatous granuloma of Tannhauser, but the entire absence of xanthomatous lesions in the skin and other characteristic sites and the small amount of lipid in the foam cells make such a diagnosis improbable. Other conditions giving a rather similar histological appearance, such as histiocytoma and tendon sheath tumour, can be excluded clinically, and there is nothing to suggest that the lipid-containing foam cells are merely a secondary phenomenon such as may occur in any tumour.

Dr. H. HABER : The striking feature is that the changes take place in the subcutaneous tissue. Histologically the lesion lies within the subcutaneous area and consists of reticulum cells in different stages of maturity, with storage of fat. Giant cells of the Dorothy Reed type and all types of inflammatory cells could also be demonstrated. If one considers that the fat tissue takes its origin from the reticulo-endothelial system, one can assume that we deal in this case with an anaplastic tumour of the fat, and consider the case to be lipoblastoma. I have not seen a picture like this before.

Sclerosing Lipogranuloma.—Dr. C. D. CALNAN and Dr. H. HABER (for Dr. J. E. M. WIGLEY).

S. D—, female, aged 33.

History.—November 1940 : She was admitted to West Middlesex Hospital observation ward and transferred to Springfield Hospital, Tooting, because of an acute schizophrenic episode associated with the puerperium. Apparently the present skin lesions developed after this time, though it is difficult to be sure whether they appeared within a few weeks or months or several years later. The injections she received when in hospital were morphia and hyoscine in aqueous solution.

She says that she has sometimes applied oil for insect bites on the arms and legs.

All the present lesions seem to have arisen at much the same time, and there has been no progression or new eruption since she was first seen three years ago.

There was no fever or malaise.

On Examination.—Mental retardation is evident. On the extensor surfaces of the arms and forearms is a more or less symmetrical distribution of bluish indurated and lumpy lesions of the dermis. They vary in size up to 5 cm. in diameter. Several of them are altered by biopsy scars. They are fairly well defined, and there are no nodules distributed along the lymphatics, nor enlarged lymph glands.

On the extensor aspect of the thighs, and slightly on the shins, are similar symmetrical lesions, but the majority of these show atrophy of the epidermis with a mottled yellow surface and fine vessels, simulating necrobiosis lipoidica or scleroderma. They do not extend to the buttocks or any part of the pelvic girdle area.

Investigations.—*Plasma proteins*: Total 6.2 g./100 ml. Albumin 3.1 g., globulin 2.8 g., fibrinogen 0.3 g.

Histology.—*Left arm*: The epidermis shows slightly thickened stratum corneum of basket-weave type. The stratum granulosum consists of one layer. The stratum spinulosum is slightly acanthotic and the papillary body is well developed. The collagen shows distinct thickening and homogenization of its bundles, but appears in some places normal. The striking feature of the case is the presence of numerous cysts of different sizes, giving the section a "Swiss cheese" appearance. The cysts show the following characteristics: some appear to be round holes surrounded by collagen, some appear to be lined, endothelial-like, by a single layer of flat cells. Some of the lining cells show distinct vacuolation, or foamy appearance. Deeper towards the subcutis there are many large cysts surrounded by concentric rings of homogenized cellular collagen. The arrangement of the collagen is that of onion-skin shape. There is also a granulation tissue, chiefly arranged round blood-vessels and sweat-ducts consisting of loose and dense foci of lymphocytes, large vacuolated histiocytes and a few mononuclear and multinuclear giant-cells, with a foamy and vacuolated protoplasma. There are also numerous little vacuoles interspersed with the granuloma tissue somewhat resembling the structure of leproma. In addition to this, numerous plasma cells are demonstrable, and they show different stages of degeneration leading to the formation of Russell bodies.

Left thigh: This section shows a similar appearance but for patchy extreme atrophy of the epidermis leading almost to erosion of the surface of the corium. Within the corium the large onion-skin shaped fibrotic rings round the cysts are missing. The granulation tissue is somewhat more developed. There are a few giant cells exhibiting typical asteroid bodies.

Comments.—It is impossible to obtain a precise and consistent history from this patient because of her mental retardation. This has been a major obstacle to the more thorough elucidation of her disease.

Although I have used the term lipogranuloma, I believe that my patient's condition should be separated from that of Dr. Anning's case shown here in November 1951, and which was similar to the group described by Smetana and Bernhard (1950). All of those, except one, involved the genitalia and pelvic region. I have seen two cases similar to mine in Leeds under the care of Dr. J. T. Ingram and Dr. A. J. E. Barlow. Others have been presented as scleroderma or paraffinoma. Much of this subject has been discussed in a recent monograph by Blanc of Geneva (1951), who has called them *Liposcléroses Nodulaires Dysprotéiniques*, since he regards the serum protein changes of primary importance.

The fat involved in the lesion in this case is abnormal in that it does not stain with osmic acid, and there is increased lipase activity over the area of the granuloma. There is no evidence of spontaneous resolution.

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Urticaria Pigmentosa : Beneficial X-ray Treatment. —Dr. W. J. O'DONOVAN.
Mrs. A. G—, aged 48.

I saw this patient first in 1946 and again in October 1948, when any medical treatment I had advised her doctor had shown no result. She then exhibited a very close dotting of her skin from the neck to the ankles, with darkly pigmented, discrete, largish, smooth papules and some few scarlet and pink. On each occasion I made the diagnosis of urticaria pigmentosa and the diagnosis was confirmed microscopically.

X-ray treatment was started on 7 October 1948. At first $\frac{1}{2}$ of a Sabouraud B tint with a .5 aluminium filter to a marked area on the left forearm and it was thought by both doctor and patient on 28 October that there was some improvement. In November and December three doses, each of $\frac{1}{6}$ S.B, were given at fortnightly intervals to the backs of the knees, calves and backs of the hands. In February 1949 a similar dose was given to her neck at the same intervals. In April 1949 $\frac{1}{2}$ S.B was given to the left arm and forearm, and on 2 May 1949 a notable difference between the treated and untreated skin was recorded.

At the end of July 1949 four applications of thorium X varnish were applied to the thighs and there was improvement no more, if anything a little less, than was remembered from previous x-ray therapy. On 8 December 1949 the patient's appreciation of the almost clear condition of her neck was noted. On 6 March 1950 a thorium X erythema was produced outside her left upper leg, which had never been noticed after x-ray treatment. This became brown and then faded.

It is perhaps worth recording that in May 1950 the patient said she had used a great quantity of soda in the spring cleaning without ill effects.

On 19 April 1951 $\frac{1}{3}$ of a Sabouraud B tint was given to the fronts and backs of the forearms, backs of the hands, to the neck and to the upper chest in front, which meant nineteen exposures. On 12 July the calves and thighs received $\frac{1}{3}$ S.B dose. On 18 October inside of each knee was similarly treated, and lastly on 27 March 1952 both sides of the neck and inside the left leg received $\frac{1}{6}$ S.B.

She has had no further x-ray treatment. It is to be noted that every one of these widely spaced x-ray treatments was given at the patient's urgent desire. The photograph shown is singularly encouraging when one recalls that the text books are uniformly pessimistic as to the effect of x-ray therapy, and I do suggest that it be tried on patients of mature years.

I have commenced such treatment on two infantile cases, but have not been encouraged to proceed by the complete absence of any beneficial record.

Dr. R. P. WARIN : My colleague Dr. C. D. Evans had a case of adult urticaria pigmentosa, which has been watched for three or four years and has gradually got better without any x-ray therapy. The degree of improvement was about the same as in Dr. O'Donovan's patient.

Dr. A. D. PORTER : I also have had a case of urticaria pigmentosa, a woman aged about 40, and in two years every single lesion disappeared without treatment.

Ichthyosiform Hyperkeratosis with Malignant Glands.—Dr. L. FORMAN.

Male, aged 56.

Five months' history of the skin becoming dry and harsh, and at the same time he noticed enlarged left inguinal glands.

There is a well-marked ichthyosiform change over the whole of the body, sparing the flexures of the groins and behind the knees.

The gland of the left inguinal region is enlarged and hard and suggests secondary carcinomatous glands.

Dr. Navasquez's report on an excised gland was a reticulum cell sarcoma of a dichthosyncytial type.

The blood count, vitamin A blood level (146 i.u. 100 c.u.) and serum protein bound iodine (9 mg./100 c.c.) were normal.

Dr. H. R. VICKERS : Hodgkin's disease can manifest itself as ichthyosiform dermatitis. We had a case in Sheffield of true Hodgkin's disease with this ichthyosiform dermatitis, and a case was described by Glazebrook, A. J., and Tomaszewski, W. (1944), in *Arch. Derm. Syph. Chicago* 50, 85.

Norwegian (Crusted) Scabies.—Dr. D. S. WILKINSON.

R. S—, aged 9.

This boy, a Mongolian mental defective, was admitted to hospital in January when he was noted to have considerable crusted lesions on the hands and feet, scalp and ears, and a distortion and discoloration of the toe-nails. Previous history is difficult to obtain, but he has certainly had these lesions for a good many years. After an initial period in bed for assessment, he was transferred to another block in the hospital and in the next three months 11 cases of scabies appeared in this block.

I first saw him a month ago when he showed—

- (1) Thick encrustations running exactly along the line of the wrist of both hands.
- (2) Similar lesions on the feet, particularly round the heel, and scattered to a similar degree on the hands and feet.
- (3) Mild dystrophic changes of the finger-nails of an eczematous type. Black discoloration, distortion and crusting of all toenails.
- (4) Crusted lesions on the ears, in the scalp and one or two on the buttocks. There was an underlying chilblain ulceration of the tips of the ears.

A number of the most prominent sites of encrustation have been cleared, and the hands now show scattered lesions not unlike those of ordinary scabies. The feet still show the characteristic appearance of crusted scabies, and there are lesions in the scalp. He has some scattered lesions on the buttocks.

Scales taken from the feet teem with acari and ova in all stages of development. These are also present in scales from the scalp lesions and from scrapings of the nails. Biopsy taken from the wrist shows the "sponge-like" appearance of the grossly thickened horny layer, which is honeycombed with burrows, containing acari and ova sectioned in every plane. Apart from this infestation the patient shows the typical soft skin of the Mongol, with cyanotic hands and feet and chilblains on the ears. He scratches very little, but like many Mongols, is more inclined to pick the lesions.

He had an impetigo of the face two weeks ago, which cleared up with chloromycetin cream. He has had no antiscabetic treatment.

Another case of Norwegian scabies was found in the same institution three years ago. These lesions are still active.

A blood count on 12 May 1952 was within normal limits, with an eosinophilia of 3%.

Fresh preparations showed many acari and ova and biopsy showed gross hyperkeratosis and parakeratosis and the typical spongy appearance of the horn caused by the burrows, in many of which lay mites. One of these burrows can be seen penetrating as far as the stratum mucosum.

Comment.—When this case was first seen the remarkably localized hyperkeratosis of the hands and feet and scalp and the appearance of the nails was very similar to the description of Boeck's second case of Norwegian scabies. Few cases have been described in England until recently, but Dr. Ingram and Dr. Calnan have separately recorded cases. The vast accumulation of mites and the absence of a pruritic reaction suggest that in these few patients the acarus is a saprophyte rather than a parasite, and no allergic reaction is developed. Most of the cases have been recorded in Mongols, but several Mongols were among those who contracted scabies from this patient: all showed the lesions of the ordinary disease.

My thanks are due to Dr. J. M. Crawford for permission to show this case.

The PRESIDENT: I believe I showed the only other case of this condition that has been presented at these meetings. The toe-nails were principally affected, and the clinical diagnosis of ringworm infection was first made, but immediately corrected by microscopical examination of the nails.

Striate Lichen Planus.—Dr. HAROLD WILSON.

A. V—, aged 68, widow.

History.—Six months ago this patient noticed an itching patch on the front of the left wrist. Soon afterwards a few papules appeared on the back of the right hand and at the same time her tongue became sore.

The original lesion on her wrist spread downwards towards the fingers and upwards to the elbow in the form of a narrow band. The spread was gradual, and it took about three months to reach its present length.

Past history.—No previous skin disease; no serious illnesses.

Family history.—Mother died of old age; father died of chronic bronchitis, aged 51. Two sisters and one brother alive and well. Two sisters died in infancy; one brother killed in an accident.

On examination.—There is extensive lichen planus of the tongue and buccal mucosa. On the backs of both hands and forearms are scattered lichen planus papules. A narrow band of lichen planus papules extends from the proximal phalanx of the fourth finger to a point about 3 in. below the left elbow.

Biopsy. Section shows hyperkeratosis with flattening of the epidermis and obliteration of the interpapillary processes. In the superficial part of the dermis is a dense infiltrate consisting of lymphoid cells and polymorphs. There are small areas of degeneration of the collagen.

Compatible with lichen planus.

Lichen Striatus.—Dr. HAROLD WILSON.

W. J. M—, male, aged 44.

History.—For three years this patient has had a few small scaling patches on the fingers, backs of the hands, and dorsal surfaces of the feet. These are generally better in hot weather than cold, but have never produced gross discomfort. Occasionally, there has been fissuring and weeping of some of the patches. Following superficial x-ray therapy there was a remission lasting six months in 1949.

Two months ago a scaling patch developed on the back of the left wrist; this spread rapidly up to the elbow, and has persisted since then as a narrow band stretching from the wrist to the elbow. There has been no weeping, and only slight itching of this lesion.

Past history.—No previous illnesses. Recently passed A.1 on routine examination.

Family history.—Mother alive and well; father killed in first war. One sister and one brother alive and well.

On examination. There are several small scaling patches on the sides of the fingers. A single band of erythema and scaling about $\frac{1}{2}$ in. wide stretches from the back of the left hand up the arm on to the inner side of the left elbow.

Biopsy.—Section shows skin and dermis in which there are focal collections of inflammatory cells.

Two months ago a case of lichen striatus was presented at a meeting of this Society (Seville, 1952), and the relationship between lichen striatus and striate lichen planus was considered in the subsequent discussion. I have brought these two cases here to-day in order to demonstrate the differences between them, which may be summarized as follows:—

	Striate Lichen Planus.	Lichen Striatus.
Onset . . .	Gradual	Rapid.
Course . . .	Many months	Usually 8–10 weeks.
Symptoms . . .	Itching	None.
Appearance . . .	Papular. Characteristic of lichen planus	Papular and erythematous. Not characteristic.
Histology . . .	Typical of lichen planus	Non-specific inflammatory changes.
Köbner phenomenon.	Present on biopsy scar	Absent. Clearance of lesion round biopsy scar.

Lichen striatus may be a linear form of eczema, but the absence of a vesicular stage, the lack of itching and the self-limited course are unusual in an eczematous condition.

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Primary Tuberculous Complex.—Dr. BRIAN RUSSELL.

David H—, aged 6½.

Family history.—The boy's mother has pulmonary tuberculosis with positive sputum. The father is said to have had a cough for years but will not have his lungs x-rayed. One brother aged 16 and one sister aged 4 of the 8 siblings are known to be tubercular.

History.—14 March 1952.—He attended the Tuberculosis Dispensary and was noted to be fit and well.

19 March. He attended hospital with a history of a painful swelling above the right eyebrow, of about 1 week's duration. The condition was thought to be a discharging boil, with preauricular lymphadenitis. There was also conjunctivitis on the right side.

23 March.—As the boil had not resolved a course of penicillin was begun but the lesion did not respond. Later an area of inflammation, swelling and scabbing developed around a central superficial ulcer.

During these attendances temperatures between 98·6° and 101·0° F. were noted.

Condition on examination (13 May). Gross enlargement of right preauricular gland. Superficial ulceration with surrounding crusting and erythema over the middle part of the right eyebrow, with some loss of hair.

Skiagram of chest normal on 24 July 1950 and 14 March 1952.

24 July 1950 : Tuberculin jelly patch test negative (60% old tuberculin).

20 June 1951 : Ditto, slightly positive (95% old tuberculin).

13 May 1952 : Ditto, positive (60% old tuberculin) : vesiculation and infiltration.

Comment.—Hellerström (1951) reported 6 cases which he regarded as inoculation lupus vulgaris following abrasions received in swimming baths. The lupus vulgaris developed immediately from the tuberculous chancres. He believes that high degree allergy developing with particular rapidity owing to superficial cutaneous abrasion inoculation leads to the development of this inoculation lupus vulgaris.

My patient is, I think, not of this category but of deeper inoculation. I recently saw a boy, however, with lupus vulgaris on the knee and inguinal lymphadenopathy which had followed a primary tuberculous chancre on the knee.

REFERENCE.

HELLERSTRÖM, S. (1951) *Acta derm.-venereol. Stockh.*, **31**, 194.

Leucoderma and Psoriasis.—Dr. STEPHEN GOLD.

Mrs. D. H—, aged 70, suffers from diabetes and osteoarthritis of the spine.

She has noticed white patches on her skin for over thirty years : chronic psoriasis developed after removal of her gall bladder in about 1927. These psoriatic patches, since the onset, have been localized to the leucodermic areas.

Past medical history.—Rickets as a child.

She has had 11 normal pregnancies and 4 miscarriages.

In 1927–1930 she suffered from nephritis, cystitis and cholecystitis.

In 1936 she developed the first symptoms of diabetes. It was definitely diagnosed in 1937.

In 1949 a myocardial infarction.

On examination she is a plump old lady. The leucodermic patches are scattered over her body, but particularly on the hands, forearms, abdomen, face and back. Patches of chronic psoriasis are largely limited to these leucodermic areas, though in places there has been a slight spread of the psoriasis on to normally pigmented skin.

Dr. GOLD : I wish to emphasize that this patient had leucoderma for 20 years, and when the psoriasis appeared it remained confined to the depigmented areas.

The following cases also were shown :

(1) Erosive Gingivitis Lichen Planus of Mouth and Vulval Skin. (2) Morphoea-like Epithelioma.—Dr. L. FORMAN.

(1) Cutaneous Eruption in a Patient with Filariasis Loa-loa. (2) Case for Diagnosis.—Dr. J. S. PEGUM.

Pityriasis Rubra Pilaris.—Dr. P. J. FEENY.

OBITUARY.

DR. J. A. DRAKE.

JOHN ALEXANDER DRAKE was born in Clifton, Bristol, in 1878. His earlier education was received at Malvern College and he entered King's College, London, as a medical student at the age of eighteen. He took the Conjoint Diploma from King's College Hospital in 1902, thereafter obtaining the post of house surgeon to Sir Watson Cheyne. Dr. Drake was thus one of the last remaining men whose contact with Lord Lister's work was direct. He took the London M.B. the following year and was at that time honorary secretary of the Medical Society of King's College.

He spent the years between 1905 and 1915 in general practice at Tenby, Pembrokeshire. This had been forced upon him by ill health, though it was disappointing to one who had won the Warneford and Junior Scholarships and the Sambrooke Exhibition whilst at hospital. Whilst in practice he took great interest in dermatology, an interest which then began to mould his future.

His health did not allow his participation in the 1914-18 war as a member of the Forces, but he succeeded in getting into the 4th London General Hospital as the civilian director of a Medical Division. That hospital was in fact King's College Hospital, which had moved out to South London a few years before and which then found itself expanded into a huddled hospital occupying Ruskin Park. This appointment allowed Drake to renew his acquaintance with the Skin Department, then under the control of the late Professor Arthur Whitfield. This association bore fruit in 1919 when Drake was appointed clinical assistant to that Department. The years 1919 and 1920 saw the attainment of both the D.P.H. and the M.R.C.P., after which he became Assistant Physician to the Department and also Director of the V.D. Department in succession to the late Dr. d'Este Emery. He became full Physician in 1927, the year during which Arthur Whitfield retired. He remained at King's for a further ten years, eventually retiring in 1937 and being then made Consulting Physician and Emeritus Lecturer in the Medical School. He was elected a Fellow of the Royal College of Physicians in 1926.

Although he was himself not a prolific writer he acted as Assistant Editor of this Journal for many years, mostly whilst Dr. Roxburgh was Editor. Of his own papers perhaps that on the Eczema-Asthma-Prurigo Complex was best known. This was read at the Annual Meeting of the Association in Oxford in 1928, immediately following the opening of the discussion by the late Dr. Cranston Low. He also served as Honorary Secretary to the Section of Dermatology of the Royal Society of Medicine, and was one of the very few dermatologists to serve as Examiner in Medicine to the Conjoint Board.

His interest in his hospital was great, and he was Vice-Dean of the Medical School for about twelve years before he was elected Dean in 1932, which post he held until his retirement. His annual re-election to that post is in itself proof of the faith placed in him by his colleagues: it also demonstrates that he was well liked by the students themselves. His tenure of office saw the completion of the new buildings of the school.

In character he was quiet and unassuming. Even during the worst phases of his chronic ill health he never allowed it to warp his kindly outlook. He was greatly liked by his fellow dermatologists and many expressions of regret have been heard since he died in his own hospital on 29 October. He married in 1908 Lorna, daughter of Mr. C. J. Stewart, to whom we extend our very real sympathy.

CORRESPONDENCE.

To the Editor of 'The British Journal of Dermatology.'

SIR,

CONGENITAL PILAR DEFECT SHOWING FEATURES OF PILI TORTI.

I was interested to read this article by Dr. J. Martin Beare (*Brit. J. Derm.*, **64**, 366) as the condition resembles an Italian family presented by me, with Dr. W. N. Goldsmith's permission, at the Annual Meeting of the British Association of Dermatology in July, 1946. Since the cases did not conform to the classical picture



FIG. 1.



FIG. 2.

of Pili torti we used the title "Pili torti cum Alopecia." Further, since the cases shown at that meeting were never published, perhaps I might be permitted to record a summary of this rare familial abnormality.

The mother aged 40 and her two sons aged 10 and 13 were affected, while the hair of her husband and daughter was normal. The alopecia varied in severity from slight loss in the younger boy, who had coarse auburn hair, to almost complete baldness in the case of the mother (Fig. 1), who, like her elder son, had coarse black hair. Although

the alopecia was non-cicatricial, "exclamation mark" hairs were never seen. The adjacent hairs could be easily withdrawn, and many retained their root sheaths. Most hairs showed twisting of varying degree and incidence, and some were fractured. Cross-sections of the hair-shafts showed no flattening. The lateral halves of the eyebrows were sparse, but the hairs untwisted. While there was paucity of body hairs in all my cases, the nails were of normal texture and there was no mental retardation.

I observed these patients for some years and found that the younger boy, who developed the disease at the age of 9, made a spontaneous recovery around the time of puberty. The alopecia of the older boy, which started when he was 11, had doubled its area in three years and has since extended at a slower rate. The condition of the mother, who first noticed it when 18 years old, remains unaltered.

Histological sections from the older boy's scalp showed complete disintegration of the hair-follicle at its deepest portion, with a foreign-body giant cell reaction scavenging pieces of the developing hair-shaft (Fig. 2). The appearances were comparable to Civatte's classical description of pseudopelade of Brocq except that the initial retrogressive process was around the papilla and not in the superficial part of the follicle as in pseudopelade. This might account for the presence of scarring in the latter disease, and its absence in my cases.

My theory on the development of hair twisting in these cases has not altered since 1946, and I should like to quote it: "Since the more advanced changes are found in the hair papillae, it is reasonable to assume that the disease starts here. These retrogressive changes must seriously interfere with the process of hair formation. This would cause a retardation of growth at a point on the hair matrix which caps the papilla, which, in turn, would lead to an irregularity of speed in the production of formed hair elements. The unaffected portions of the matrix, which would be producing hair at a normal (and therefore relatively faster) rate, would bend over towards the affected zone and thus the resultant hair-shaft would be bent. This discontinuous process may affect at different times different sectors of the hair matrix, and thus cause not only bending but twisting of the hair. Furthermore, it must be remembered that after it is produced the hair is constantly being pushed into a comparatively rigid cylindrical follicle, which cannot accommodate severely bent hair: Thus the shaft must twist."

I am, Sir, Yours faithfully,

I. MARTIN-SCOTT, M.D.

London, W. 1;

7 November 1952.

BOOK REVIEWS.

CARDIOLIPIN ANTIGENS.*

SINCE the introduction of serological tests for the diagnosis of syphilis in the early part of the century many improvements in technique have been made, both as regards complement-fixation procedures and the newer flocculation and precipitation methods. Until 1942, when cardiolipin was isolated by Pangborn and her associates, little advance had been made in the preparation of the necessary antigens. Empirical methods, followed by a long series of comparisons with an accepted antigen remained current practice. Since the isolation of cardiolipin it has been shown that a greater

* *Cardiolipin Antigens.* By MARY C. PANGBORN, F. MALTANER, V. N. TOMPKINS, T. BEECHER, W. R. THOMPSON and MARY ROSE FLYNN. World Health Organisation: Monograph Series No. 6. Pp. 63. Price 5s.

degree of sensitivity can be achieved, and a smaller number of biological false positive reactions encountered, if standardized cardiolipin antigen is used. The present publication deals with the whole subject of cardiolipin antigen, and is a most important step towards the complete standardization of serology in syphilis. The publication is issued by the World Health Organisation, in continuation of work started by the Health Organisation of the League of Nations, which carried out extensive controlled experiments to test the efficiency of different serological methods in the years between the two world wars.

To those concerned with technical methods the present work is important. However, future editions might well provide some explanation of the formula given on p. 34, and it would be more helpful also if reference were made in the text to the extensive bibliography quoted. The inclusion of a summary in French and English is helpful, and might well be copied in other highly technical monographs. J. O. O.

THE IBERIAN-LATIN AMERICAN CONGRESS, 1950.*

THE first Iberian-Latin American Congress of Dermatology and Syphilis properly began by defining the nomenclature of diseases, and the report of a commission appointed by the Brazilian Society was presented. Agreement with their recommendations will be general.

The next paper in the proceedings shows how rash it is to assume that there is uniformity in defining elementary lesions. Parallel lists show differences not only between one country and another, but also between one book and another in the same tongue. Even in this country everything is not "according to C(rocker)." The authors of the paper hold that lesions should be classified according to their morphology without considering their aetiology, pathology and evolution. A list of rare and new eponyms contains many that it would be better to let perish by neglect.

The second section of clinical, histological and experimental papers are all classified under the broad heading of cutaneous allergies, and the final section is allotted to syphilis. G. W. B.

CURRENT LITERATURE.

A SINGULAR STEATOGENOUS BASALIOMA. D. HOFFMANN. (1952) *Derm. Wschr.*, 125, 459.

The author describes a minute "rodent ulcer" at one outer canthus seen microscopically to arise from a sebaceous gland. Of particular interest histologically was the honeycomb-like layer walling off the lesion; and stretched over this a thin narrow band reminiscent of an argemone membrane—becoming red on drop staining with giemsa-glycerine (1:6-8): in the course of days to weeks the intervening tissue dyed also an astonishingly deep red. M. S. S.

LICHEN AMYLOIDOSUS WITH THE CLINICAL APPEARANCE OF LICHEN VERRUCOSUS CHRONICUS VIDAL. H. WEYBRECHT. (1952) *Derm. Wschr.*, 125, 460.

An apparent lichen verrucosus of both lower legs and later of thighs and arms in a man aged 72 proved microscopically to be lichen amyloidosis. Of almost a year's duration the eruption consisted mainly of intensely itchy warty nodules of pin-head size. Only with Freudenthal's modification of the congo red stain was it possible to demonstrate amyloid. Staining with cresyl violet revealed numerous very granular mast cells related mainly to amyloid deposits and blood vessels: many prickle-cell nuclei were deformed or failed to stain, and numerous homo-

* *I Congresso Ibero-Latino-Americano de Dermatologia e Sifilografia*. Rio de Janeiro, 1950. Published for the Brazilian Society of Dermatology and Syphilis.

geneous round inclusions about the size of 1-2 prickle cells suggested the "intra-epidermal" amyloid of Freudenthal and stained orange red with congo red (as described above). Areas of liquefaction also were present in the epidermis, and a subepidermal cleft presented above the amyloid deposit and extended almost throughout the whole individual nodule. Flat hyperkeratosis of elbows and knees suggested a constitutional tendency to hyperkeratosis. Photographs and microphotographs accompany the text, with detailed histology and biochemical findings.

M. S. S.

TREATMENT OF FRESH KELOIDS WITH HYALURONIDASE. O. BRAUN-FALCO and G. WEBER. (1952) *Derm. Wschr.*, 125, 465.

As a result of their further experience the authors are in a better position to judge the indications for and usefulness of hyaluronidase treatment. It has been shown that in fresh keloids masses of large mast cells are present, and it is suggested that mast cells are the origin of hyaluronic acid.

The authors now find that only fresh keloids respond well to hyaluronidase (of not more than $\frac{3}{4}$ -1 year), and not older ones rich in collagen fibres. Scleroderma like older keloids does not respond well. Differing in this respect is scleroedema adutorum (Buschke): here a marked increase in hyaluronic acid and many mast cells are found.

The authors use mainly Apertase (Hoechst) but also Kinetin (Schering) and Luronase (Bayer)—infiltrating the whole keloid by several injections (2-3 usually) of about 1 c.c. aqua dest. containing 100-200 units of hyaluronidase. The first injections are usually painful, and are followed by lively redness and a more or less severe inflammatory reaction. After 5-10 days the keloid becomes insensitive and more vascular and later appreciably softer. Injections given daily at first are later spaced out and the duration of treatment lasts as a rule 6-8 weeks. In several cases extensive keloids completely retrogressed in a short period but not all fresh keloids respond.

M. S. S.

SKIN THERMOMETRY AND OSCILLOMETRY IN THE PROGNOSIS OF ULCUS CRURIS.

H. GABRIEL and A. LUGER. (1952) *Derm. Wschr.*, 125, 485.

Oscillometry is found by experiment to be of value, but skin thermometry of none in the prognosis of ulcus cruris. The prognosis is best when normal values are obtained with oscillography both at work and at rest even with hardening of the veins. A reduction in healing tendency is found with disturbed oscillography findings and appears to be directly proportional to the degree of arterial derangement. In all 102 patients were investigated: 60% showed arterial derangement and 8 of these also a venous, although there was no evident varicosity.

M. S. S.

DISEASE OF SKIN, MUCOUS MEMBRANE, PROSTATE AND EPIDIDYIMIS INDUCED BY PENICILLIN AFTER SENSITIZATION WITH A YEAST-LIKE FUNGUS (CANDIDA GROUP). D. JANKE. (1952) *Derm. Wschr.*, 125, 525.

The author describes aggravation of a coincidental monilia infection (e.g., groins, finger-nails, interdigital webs of toes or tongue) in several patients following therapy with large doses of penicillin; and a penicillin eruption of varying degrees of severity, but extensive severe and vesicular or bullous in several of his patients, as a rule appearing after the 6th-14th day of treatment. Of two further patients, one a syphilitic developed prostatitis and the other under treatment for gonorrhoea, epididymitis following penicillin therapy and in both on investigation *Candida albicans* was found on culture. Experimentally the author found that the growth of monilia from the skin was greater, and that of the accompanying banal skin organisms was less, following penicillin therapy. *In vitro* tests showed no evidence that penicillin directly stimulated the growth of monilia. He points out that intracutaneous tests, e.g., to monilia, are more likely to be positive if carried out close to the area of infection and may be negative at a distance. Altogether 11 patients were investigated.

M. S. S.

PHLEBITIS AS THE CAUSE OF SUBCUTANEOUS CALCIFICATION. B. LINDNER. (1952) *Derm. Wschr.*, 125, 211.

The author points out that calcification is probably always a secondary development, and cites from the literature some primary causes (he gives very many references), but he has not found any specific mention of phlebitis as a precursor. He describes subcutaneous calcification (revealed by skiagram) associated with varicose veins of both legs, and a palpable phlebolith in a woman aged 75 with a history of many attacks of phlebitis of both legs dating back 50 years.

Analysis of a bean-sized concretion present $\frac{1}{2}$ cm. below the ulcer crater of one leg revealed an organic core of necrotic collagenous fibres and fat tissue; at the margin of the necrosis a metaplastic new bone formation; a preponderance of phosphorus over carbon compounds. The ulcer healed rapidly on removal of the foreign bodies. The local asphyxia resulting from diseased veins would result in increased calcium solubility followed by alkalotic metabolic changes from resulting cell damage with deposition of calcium salts.

M. S. S.

CUTANEOUS RETICULO-HISTIOCYTOSIS WITH MELANODERMIA. R. FRÜHWALD. (1952) *Derm. Wschr.*, 125, 217.

The author describes cutaneous reticulo-histiocytosis with melanoderma in a woman aged 59 who reported that she had had severe itching for 10-12 years before the onset of "eczema." Pigmentation appeared early and gradually spread over the whole body, sparing the face, and was diagnosed at first as Addison's disease. Alopecia developed suddenly, leaving only a band of hair at the occipital margin, and following periungual bolstering the nails fell off. Glands were enlarged, and in addition to the general thickening and atrophy of the brown red and slate grey skin, small bean-sized infiltrations were present on the arms. A leucocytosis of 14,000 (unusual in this complaint) with 53% of lymphocytes was present. The author thinks such cases are not infrequently wrongly diagnosed from omitting to stain the skin for argentophil fibres. Skin and lymph gland here showed a fine argentophil reticulum. There was no enlargement of liver or spleen. The author suggests that this may not be a disease entity, but a special histological reaction of the skin which may on investigation be found in all cases of erythrodermia; or if not, then by argentophil staining it may be possible to differentiate further the various types of erythrodermia.

M. S. S.

PERCUTANEOUS INFLUENCE ON AUTONOMIC REFLEX PROCESSES IN THE SKIN. R. SCHMITZ and G. W. KORTING. (1952) *Derm. Wschr.*, 125, 292.

The authors find by experiment that pendiomid (a ganglion blocking substance) massaged into the skin of the flexor surface of the forearm for 2 minutes in a 1% strength in lanette wax base can reduce the reactivity of the skin to the intracutaneous injection of histamine, adrenaline and sympatol and increase that to acetylcholine. This is in keeping with pharmacological experience of its vagotonic tendency.

M. S. S.

A REMARKABLE SKIN CHANGE FROM CONTACT WITH HEXACHLOROCYCLOHEXAN (NEXIT) AND BRENZAKATECHIN; AND THE PROBLEM OF CHROMIDROSIS. W. WOHNICH. (1952) *Derm. Wschr.*, 125, 299.

A patient with Graves's disease who suffered from severe hyperidrosis and who worked with Nexit and Brenzakatechin developed many pinhead to lentil-sized hollow skin defects over the palms with blackish-brown discoloration. A crystal of the gamma isomer of Nexit was observed microscopically as it lay on the patient's palm, and was found first to become a bright brown-red colour and later to become lodged in the superficial horny layer, being only with difficulty scratched out. The red-brown colour later changed to black, reminding one of the dopa reaction. The Nexit was now tested with normal sweat obtained with the aid of a heat bath. After several hours in a water-bath at 33° C. a light blue-violet colour appeared. A similar reaction was obtained with traces of dopa or Brenzakatechin but more quickly and deeper in colour. Tyrosin gave no such reaction. This suggests that the sweat contains dopa oxidase but not tyrosinase. Sweating in workers with Nexit and Brenzakatechin is accompanied by a noticeable smell of the compounds (bromidrosis). The skin discoloration in workers can be made to disappear completely with potassium permanganate solution.

M. S. S.

THE ACTION OF PENICILLIN ON COLONIES OF COMMON DISEASE-PRODUCING DERMATOPHYTES. A. DÓSA. (1952) *Derm. Wschr.*, 125, 337.

In a series of experiments the author found that penicillin was ineffective against fungi pathogenic to the skin except in doses larger than those used in therapy; even then only slightly, and only against the most slowly growing fungi, e.g., *Achorion schonleini*. It is possible that fungi, like bacteria, can produce penicillinase.

M. S. S.

KELOID ORIGIN. W. Hörs. (1952) *Derm. Wschr.*, 125, 361.

In the aetiology and pathogenesis of keloids dispositional factors such as heredity or tuberculosis and exogenous causes, e.g., the type of injury and its duration, usually enter into con-

sideration. In reviewing in the literature the skin affections which have been followed by keloid, the author notes that the lesions are usually to a greater or less extent flat, and that even trauma mainly in a sagittal direction on the skin, as a cut or stitch, could be influenced by secondary factors, e.g., spread of infection laterally or spread of fluid by injection. He notes also that the affections mentioned reach a certain depth, to the stratum papillare, or stratum reticulare; that their extent or complications lead to slow healing and that they are localized over a bony or cartilaginous area lying at some depth. In studying a series of cases of his own of keloid scarring following removal of pigmented naevi with the rasp the author finds that the same factors apply. Where pigment lay deeper or the naevi were hairy, demanding deeper scraping, keloid scarring was more apt to follow, although the rest of the scar might remain keloid free. Surgical removal of the keloid was followed by no recurrence. The wound following treatment of a naevus was often saucer sized and the centre was the slowest part to heal; it was found that keloid scarring was usually in the centre of a large scar. The histology of spontaneous keloids and keloid scarring is compared, but the author finds that characteristics of spontaneous keloids are present in a specimen from one of his operation cases. M. S. S.

THE MODE OF ACTION OF NOVOCAINE AND VITAMIN D₂ IN EXTRAPULMONARY TB.

H. SIELER. (1952) *Derm. Wschr.*, **125**, 392.

A patient with a papulo-necrotic tuberculide and knee tuberculosis suffered also from migraine. She was given intravenous injections of novocaine for the knee lesion since novocaine was known to have an action like calciferol: three injections of ordinary dosage were given in a period of three weeks, and during that time she had 29 convulsions sometimes two or three a day followed by sleep; they tended to occur at regular intervals of 8-12 hours.

About six weeks after cessation of the fits vitamin D₂ therapy was started, 1 mg. daily in twenty-two days, but with this the convulsions immediately recurred. They stopped on stopping the drug, but recurred again on giving it after an interval of seventeen days. Later, after an interval of three months she was able to tolerate calciferol when given combined with vitamin B complex.

The author reaches the conclusion from a consideration of his own case and another in the literature that the vegetative disturbance following novocaine arose through a brain stem effect, and that the calciferol must have had a similar effect, modified later by the giving of the vitamin.

M. S. S.

ALVEOLAR MELANOBLASTOMA OF THE SKIN WITH AMELANOTIC SKIN METASTASES AND MELANOTIC METASTASES OF THE INNER ORGANS.

K. KÖRBER and H. WEYBRECHT. (1952) *Derm. Wschr.*, **125**, 548.

The clinical, post-mortem and histological findings are described and photographs of these illustrate the text. An ulcerated nodule of the back was removed from a man aged 65 and the area was irradiated but metastases began to appear six months later, also a plum-sized and coloured swelling at the site of the operation scar (there had not previously been a biopsy and the patient could not say whether the original lesion had been pigmented). Following the appearance of metastases the urine was found to contain melanin.

M. S. S.

THE EFFECTS OF PERIPHERAL CIRCULATORY DERANGEMENTS, THE CLINICAL PICTURE OF COLD INJURIES, AND THE BEHAVIOUR OF INFECTIVE SKIN PROCESSES.

E. KEINING. (1952) *Derm. Wschr.*, **125**, 545.

Freezing differs from frost injuries which originate from peripheral circulatory derangements and may arise in temperatures little below room level, but more severe the greater the degree of frost. Autumn pernio affects first the distal lower extremities from cold rooms, spring pernio the rims of the ears and the hands (often like erythema multiforme) from working in the open in the cold early morning. Light probably plays a part in spring pernio from the warming of the frost-damaged areas by the hyperaemic action of the ultra-violet rays. Cold purpura is another type of injury in the predisposed (those with cutis marmorata particularly prone). Only the exposed parts are affected, stopping sharply at the level of the sleeve or shoe, and with its distribution over the areas of asphyxia in the mottled skin (photographs illustrate this). Infective processes are adversely influenced, as in ecthyma gangrenosum. The hyperergic forms of skin tuberculosis, papulo-necrotic tuberculide and Bazin's disease appear on areas of asphyxia or ischaemia with reduced metabolism. In such areas the Pirquet reaction is frequently negative. Bed-rest should relieve these disturbances by improving the circulation, thereby increasing resorption of toxins.

The virus of warts is more readily inoculated on acroasphyxial terrain, and the tendency to paronychia and onychomycosis in acrocyanosis is also well known.

M. S. S.

WHAT DERMATO-VENEREOLOGICAL INDICATIONS ARE THE SULPHONAMIDES STILL TO BE RECOMMENDED? *Derm. Wschr.*, 125, 268.

Sulphanilamide is still worth a trial in pemphigus chronicus, and in actinomycosis in high and continuous doses. A small percentage of erythematodes patients seem to benefit from a combination of sulphanilamide with nicotine acid amide. It is no longer indicated in furunculosis, sweat-gland abscesses or erysipelas.

Side effects are less when only sulphanilamide is used externally or internally, not sulphonamide, e.g. marfanil. We renounce the external application of sulphonamide and sulphanilamide completely and use only sulphanilamide internally.

R. Brett (*Mainz*).

The sulphonamides cost only a half to a third the price of penicillin to treat banal pyogenic skin infections, e.g., impetigo or pyoderma. Penicillin is preferable for a severe carbuncle in the absence of penicillin resistance. For erysipelas uliron is useful. Local treatment of the skin with sulphonamide salves is often superfluous and dangerous, although not so in wounds.

J. Felke (*Wiesbaden*).

The local use of sulphonamides has largely declined owing to the risk of sensitization especially with presence of an inflamed, e.g., eczematous, skin. Penicillin has sometimes an unfavourable effect on secondarily infected mycoses leading to aggravation of the mycosis; here the cheaper sulphonamide is often of value. In dermatitis herpetiformis sulphapyridine in particular is indicated. A mixture of sulphonamides is preferable where a high dosage if necessary to lessen the danger of concretions in the urinary tract.

Gosta Hagerman (*Lund*).

Sulphanilamide and its compounds are preferable to other sulphonamides owing to its fewer side effects. It is useful in superficial pyogenic skin infections, secondarily infected eczema and seborrhoeic eczema, ulcus cruris, anthrax and actinomycosis, and can be applied as moist dressings of a watery solution or water in oil salve using a pure salt of sulphanilamide. Diazine inhibits the growth of the actinomycetes. Sulphamethadiazine, 6 tablets daily for several months (total 600 g.), healed two cases of visceral actinomycosis. Sensitivity to the sulphonamides in contrast to the sulphanilamides is discussed in detail in relation to the chemistry of the drugs.

J. Kimmig (*Hamburg*).

The superficial pyogenic infections, carbuncles and sweat gland abscesses heal with the sulphonamides. Badional salve is useful in ulcus cruris. Many hundreds of cases of erysipelas have yielded excellently to protosil rubrum. The use of sulphonamide in pemphigus vulgaris and dermatitis herpetiformis have helped itching and secondary infection and lead to the healing of individual efflorescences.

R. Brett.

Sulphonamide is a remarkable protection in hydroa vacciniforme. Several children remained free from attacks for the first time with a 5-10% solution of Eleudron as a paint. The secondary infection of deep trichophyton infections heals quickly and with high doses of supronal alone early cases of actinomycosis can be healed—older infections responding best to a combination of the sulphonamide with penicillin. Erythematodes is benefited sometimes by small doses of uliron.

H. Löhe (*Berlin*).

The other antibiotics have in no way displaced the sulphonamides except for the staphylococcal infections where penicillin has unlimited sway, but in folliculitis sulphonamides in the end are often more effective than the costlier penicillin. Sulphonamide is still the first line of treatment for erysipelas.

For the local treatment of superficial mixed pyogenic infections penicillin and sulphonamide are of equal value. Sulphathiazole is particularly well tolerated, 5-10% in a lanette wax eucerine vaseline mixture; the penicillin in watery solution. This can be combined with oral sulphonamide. Ulcus cruris, x-ray reactions and healing operation wounds benefit from a 2-3% salve, also many extensive dermatoses, e.g., erythrodermia, pemphigus vulgaris, exudation eczema and secondary infected mycoses. Sulphonamide as a powder is useful in infected seborrhoeic eczema (in the form of rivanol).

H. Tn. Schreus (*Dusseldorf*).

M. S. S.

ELECTROGALVANIC CURRENTS IN THEIR PATHOGENETIC AND THERAPEUTIC ASPECT IN DERMATOLOGY. H. FRIDERICH and R. WIEHL. (1952) *Derm. Wschr.*, 125, 385.

Extensive ulceration of the mouth and tongue, at first sight suggesting tuberculosis or syphilis, was judged finally to be caused by the many dental fillings, crowns, and bridges of different metals or metal alloys in the patient's mouth. Investigations did not support a diagnosis of syphilis or tuberculosis, but measurable electrical currents were revealed arising from the presence of the metal. Ulceration was most marked at the sites of greatest concentration of metal. Oral hygiene helped considerably but did not entirely cure the condition.

The authors report their results in 63 cases of acne vulgaris of the trunk treated micro-electrically with a shower of volatilized metal ions (derived from 10 mg. of a mixture of gold and silver salts heated electrically to 1200° C.) influenced by the pH of the skin previously exposed to infra-red rays to promote sweating. The resulting complex protein compounds of heavy metal ions control inflammation and disturb bacterial metabolism. The acne of the trunk is more suitable than that of the face for this treatment.

The average duration of treatment given twice or thrice weekly was 4-6 weeks. The technique of investigations and therapy are described. M. S. S.

VESSEL CHANGES AND CLINICAL ASPECT IN ULCUS CRURIS. H. GABRIEL and A. LUGER. (1952) *Derm. Wschr.*, 125, 433.

The authors have evolved a method of analysing statistically the findings in ulcer cruris, and conclude from their experience that the rate of healing of a leg ulcer is slowest in the presence of arterial sclerosis or a functional predominantly arterial lesion, less slow with a mixed venous and arterial derangement, and best with involvement of the veins only. They do not find that the type of vessel disorder bears any relation to the number of ulcers. M. S. S.

SCABIES NORVEGICA IN A PATIENT WITH CUTANEOUS RETICULOSIS. W. HAUSER. (1952) *Derm. Wschr.*, 125, 442.

This disease is only rarely described in the world literature. In this condition instead of 10-20 or up to 100 acari as in ordinary scabies one finds millions. Itching, severe at first, is usually slight later, and there is usually some general predisposing factor to facilitate infection, e.g., imbecility, marasmus, derangement of sensibility from nervous disorder, etc., or crusted scaly dermatoses. In the case described, a man aged 63 with cutaneous reticulosis had an intensely red infiltrated and atrophic itchy skin. Under crusted scales numerous mites were found in various stages of development. Relatives of the patient had "ordinary" scabies. A year later when the scabies was well the blood serum electrophoretic pattern revealed increased β and above all γ globulin (17% and 25%), with albumin 41% of a total content of 7.77 gm.% protein, supporting, like the histology and clinical picture, a diagnosis of reticulosis. Biopsy of the swollen glands was not permitted. M. S. S.

SURGICAL CORRECTION OF LYMPHOEDEMA. G. H. PRATT. (1951) *J. Amer. med. Ass.*, 147, 1121.

The author has employed a modified Kondoleo operation in 46 cases. The results were good in 36, fair in 4 and unsatisfactory in 6. The electric dermatome has reduced the technical difficulties of the operation. A. J. R.

PERFORATED EAR DRUM FOLLOWING HOME PERMANENT WAVE. J. SATALOFF and J. F. WILSON. (1951) *J. Amer. med. Ass.*, 147, 1135.

A woman aged 53 allowed some cold-wave neutralizing solution to run into her ear and felt an immediate sharp burning sensation. An extensive antero-inferior marginal perforation was found and is considered to have been produced by the solution. After briefly reviewing the literature on cold-wave preparations, the authors suggest that instructions issued with home permanent wave sets should warn that eyes and ears must be specially protected, and that waving must be postponed in the presence of open skin lesions, excoriations or infection. A. J. R.

PURPURA AND NEPHRITIS AFTER ADMINISTRATION OF PROCAINE PENICILLIN. M. SPRING. (1951) *J. Amer. med. Ass.*, 147, 1139.

The day after receiving 300,000 units of procaine penicillin a man aged 53 developed anaphylactoid purpura with nephritis. A. J. R.